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TRANSFUSION OF BLOOD

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TRANSFUSION OF BLOOD

BY

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FOREWORD

In this volume Dr. Feinblatt has presented a critical survey of the subject of blood transfusion as it stands to-day and has arranged the text in such a manner that each chapter becomes a ready reference on the several phases of the subject.

Blood transfusion is of such great therapeutic value and has come into such general use in the treatment of various acute and chronic lesions that a volume of this type will do inestimable good and be of great value, not only to the surgeon, obstetrician and medical man but to students, internes and residents, who must necessarily, at times, do much of the technical work.

The chapters on physiology, grouping, donors and indications are clear and concise and should be read by every student of medicine.

JOHN OSBORN POLAK.

PREFACE

The subject of blood transfusion has within recent years become one of first importance. The high repute in which this procedure is held by the profession is well reflected by the large number of communications on this subject which appear in the current periodicals from time to time.

A few years back, the technic of blood transfusion was so difficult that there were only a relatively small number of workers who possessed the requisite degree of skill to perform the operation. The simplification of instruments and methods of the last few years, however, has opened the possibilities of blood transfusion to the great body of doctors all over the country.

The chapter dealing with the indications for and the therapeutic value of blood transfusion has been made as comprehensive and complete as possible. I have made an exhaustive survey of the literature on this subject and correlated it with my own experience. Likewise, in describing the methods of performing transfusion, special effort has been made to present the most important methods in proper detail.

In the preparation of this manuscript, I have endeavored to present a critical survey of the subject of blood transfusion as it stands today. The voluminous literature on this subject has been carefully gone over and sifted, and I have attempted to give due weight to foreign and American contributions alike. At the same time, I have largely been guided by my personal experience and views in the selection of material to be included in the text.

HENRY M. FEINBLATT.

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TRANSFUSION OF BLOOD

CHAPTER I

Historical Résumé of the Steps in the Development of the Modern Practice of Blood Transfusion

Introduction. In this chapter an attempt is made to outline the steps which have played an important part in the evolution of the present day practice of blood transfusion. No pretence of historical completeness is offered, as the object in view is a critical evaluation of the epochal discoveries in this field rather than a chronologic narrative of the events themselves.

As one casts a bird's eye view over the history of blood transfusion, from the description of the crude procedure employed in the first authenticated blood transfusion performed on man in 1667 to the safe, exact, and carefully controlled technic of today, he is impressed by certain historical landmarks which stand out in bold relief. It is with these outstanding features, which have made possible the satisfactory status of present day blood transfusion, that this chapter will deal.

Historical Landmarks. The outstanding contributions to the development of the modern practice of blood transfusion have been as follows:

1. The announcement of the theory of the circulation of the blood by William Harvey in 1628.
2. The successful practice of blood transfusion on animals by Richard Lower in 1665.
3. The performance of the first blood transfusion on man by Jean Baptiste Denys in 1667.

4. The employment of an indirect method, i.e., by the use of defibrinated blood, by Bischoff in 1835.

5. The discovery of the presence of iso-agglutinins in the blood by Landsteiner and by Shattock in 1900.

6. The classification of human bloods into four groups by Janský in 1907.

7. The description of a satisfactory technic for direct artery-to-vein transfusion by Crile in 1907.

8. The revival and technical improvement of von Ziemssen's vein-to-vein method with multiple needles and syringes by Lindeman in 1913.

9. The use of citrate and glucose as an anticoagulant by Hustin, and of citrate alone by Agote, in 1914; and the perfection of Agote's method by Lewisohn in 1915.

10. The introduction of an improved syringe method depending on the principle of a two-way stop-cock by Unger in 1915.

Early History. The early history of the subject of blood transfusion is vague and contradictory. Much of this confusion has apparently arisen from the fact that the drinking of human blood was during medieval times popularly considered to be a health-restorative measure. It would appear that, in the older records, transfusion and ingestion of blood were sometimes confused. It is difficult to conceive how blood transfusion could have been practiced at a time when the circulation of blood was not recognized.

It has been stated by some writers that the first blood transfusion was performed by a Jewish physician upon Pope Innocent VIII in 1492. According to this legend, the blood was obtained by bleeding three boys to death. There is no description of the method employed, however, and another version of the same event,[1] which appears more logical in view of the fact that blood was not at that time considered

to circulate, has it that the blood was administered to the pontiff as a draught.

The Theory of Circulation. With the announcement of the theory of the circulation of the blood by Harvey, it was inevitable that popular imagination, which had always attributed mystic powers of resuscitation to blood, should be directed to the devising of a method for the transference of blood from a vigorous to a debilitated subject. Harvey's epochal monograph, entitled "Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus," was published in Frankfort in 1628. Twelve years previously, however, Harvey in his lectures had formulated his theory of the circulation.

Up until comparatively recent years, three serious obstacles have stood in the way of the successful application of blood transfusion; namely, (1) blood coagulation, (2) infection and (3) hemagglutination from the mixture of incompatible bloods. For more than two centuries and a quarter these stumbling-blocks stood in the way of the successful employment of a therapeutic procedure which had been shown, in occasional instances, to yield brilliant results.

The First Transfusions on Animals.—The first successful blood transfusions on the lower animals were performed by Richard Lower of England in 1665, who connected the artery of one animal with the vein of another by means of a pipe. Lower reported the cure of a mangy dog ten days after transfusion from a healthy dog. By this means he also relieved the acute anemia of a dog which was exsanguinated following splenectomy. He performed many transfusions between animals of different species.

The First Authentic Transfusion on Man. The first authenticated blood transfusion on man was performed in 1667 by Jean Baptiste Denys of France, physician to King Louis XIV. He injected the blood of a lamb into the veins

of a youth dying as a result of repeated venesections. The patient made a remarkable recovery. The experiment was repeated on an older man with satisfactory results. In studying the effects of his blood transfusions, Denys frequently noted that the patient thereafter passed urine as black as soot. This was of course due to hemoglobinuria, resulting from massive hemagglutination and hemolysis.

With the report of encouraging results, blood transfusion was warmly received. There were many deaths, however, and finally blood transfusion was forbidden in France.

Inasmuch as there was no knowledge of the presence of iso-agglutinins in blood, or of blood groups, transfusion was at best an extremely hazardous procedure. It was advocated and used only as a last resort. The phenomena which we now know to be attributable to the mixture of incompatible blood groups, conspicuously hemoglobinuria, chills, fever and violent vomiting and purging, were vividly described in the earlier writings.

Pioneer Methods. The earlier methods of blood transfusion utilized the principle of an artery-to-vein connection effected by means of a cannula or of a system of quills. For a century and a half following the initial impetus given by the successful experiments of Lower and Denys, nothing of importance was added to the subject. There appears to have been a gradual dying of interest in blood transfusion, and there are but few references to this topic in the literature of that period.

Blundell's Apparatus. Blundell in 1818 attempted to revive the interest of the profession in blood transfusion. He invented an apparatus, which consisted of a large, funnel-shaped receptacle for the blood, connected by a two-way tap with a syringe from which the blood was injected through a tube and cannula into the recipient. Blundell's impeller was an elaboration upon this device. The syringe,

which was incorporated in one side of the funnel, contained a complicated system of spring valves designed to cause the blood to travel along the delivery tube when the piston was pushed down. The apparatus was fixed to the back of a chair for support.

Judged according to present standards, Blundell's technic was really a great deal cruder than that employed by the pioneers in blood transfusion. His clinical results were far from satisfactory. It cannot be said that Blundell's work served to improve the status of blood transfusion, except in so far as it revived the flagging interest of the profession in this procedure.

Use of Defibrinated Blood. The chief obstacle in the way of successful transfusion had always been the coagulation of the blood. In 1835 Bischoff [2] laid the cornerstone upon which the present day indirect methods of blood transfusion with modified blood have been built. Bischoff overcame the difficulty of blood clotting by the use of defibrinated blood.

Many ingenious instruments for blood transfusion were designed on the basis of this principle. Typical of them was the apparatus employed by Sir Thomas Smith [3] in 1873. His paraphernalia consisted of the following bizarre collection of utensils: a wire egg-beater; a hair sieve; a three-ounce glass aspirator syringe; a fine blunt-ended aspirator cannula, having a lateral and a terminal opening; a short piece of India-rubber tubing with a brass nozzle at either end connecting the syringe with the cannula; a tall narrow vessel standing in warm water for defibrinating the blood; and a suitable vessel floated in warm water to contain the defibrinated blood.

Fatalities attributable to blood transfusions continued to occur, and symptoms were frequently reported which we now know must have resulted from the use of bloods be-

longing to incompatible groups. Blood transfusion was used as a last resort, chiefly in the severe hemorrhages of obstetric practice, and the hazard associated with its employment was fully recognized.

The Discovery of Iso-Agglutinins in Blood and the Classification of Blood Groups. Probably the most important single discovery relating to blood transfusion was the demonstration in 1900 by Landsteiner,[4] and independently by Shattock [5] in the same year, of the presence of iso-agglutinating and iso-agglutinable substances in human blood. In the following year, Landsteiner [6] divided human bloods into three groups on the basis of their content of agglutinins and agglutinable substances.

These investigations furnished a satisfactory explanation for the severe and fatal reactions which had so frequently been observed and also offered a ready means of averting these catastrophes. The fact that the practice of blood transfusion has within the short space of a quarter of a century since this discovery attained such a high degree of technical refinement, and has become a safe and frequently performed therapeutic measure instead of a last desperate chance, is a powerful tribute to the far-reaching influence and practical value of Landsteiner's and Shattock's researches.

Janský and Moss Groupings. Janský [7] in 1907 showed that all human bloods fall within four groups. This generalization, with the exception of minor variations which will be taken up in Chapter III (see p. 25), still holds good today. Moss [8] in 1910, working independently, confirmed Janský's work, and he also made the important additional observation that iso-hemolysis of the red blood cells never occurs without their previous agglutination, although iso-agglutination may take place independently of iso-hemoly-

sis. Unfortunately, Moss, in classifying the blood groups, transposed Groups I and IV of Janský's classification, so that considerable confusion has arisen in this respect. It becomes necessary, in reporting the grouping of a blood, to state whether the classification is that of Moss or of Janský. Moss' classification has the greater vogue, but in view of priority, by three years, a committee of the American Medical Association [9] has recommended that preference be given to the Janský grouping. For that reason, the Janský classification will be used in this book.

Crile's Direct Method. The general use of blood transfusions as a therapeutic measure really dates from 1907, when Crile [10] described a practicable method for the direct transfusion of blood. Crile was to a large extent inspired by the earlier work of Carrel and Guthrie, who successfully effected end-to-end suture of blood vessels. By Crile's method, a small cannula is used, through which the vein of the recipient is drawn to be cuffed back over the tube. The donor's artery is drawn over the vein, and thus there is a continuous intima coat, leaving no rough surfaces which might cause blood coagulation. For the details of Crile's method, see page 91.

Crile conducted a large series of experimental transfusions on dogs, in addition to the many clinical applications of his method. His observations are recorded in great detail in his monograph, "Hemorrhage and Transfusion." [11] These researches have, to a large degree, furnished the basis for the delineation of the indications for and contraindications to blood transfusion. To Crile, more than to any other single worker, is the popularity of blood transfusion to be credited.

Recent Simplifications of Technic. Soon following the big impetus given to the subject of blood transfusion by Crile's work, the literature became flooded with new meth-

ods and devices for this procedure. It would be a fruitless task to attempt to enumerate them, and only those methods will be considered which have embodied new principles.

Paraffin-Coated Containers. Direct artery-to-vein transfusion entailed considerable hardship on the part of the donor, because of the necessity of severing an artery of fair size; and furthermore, there was no means of measuring the amount of blood transferred. The use of a glass cylinder with a cannula outlet, smoothly coated with paraffin in order to prevent clotting, was introduced by Kimpton and Brown [14] in 1913. For the details of this method, see page 94. The chief objection to the method of Kimpton and Brown lies in the difficulty of coating the tube and its connections with a uniform layer of paraffin, upon which the success of the procedure depends.

Multiple Syringes. The use of syringes for the purpose of transferring the blood from the vein of the donor to that of the recipient naturally suggested itself. Von Ziemssen [15] had in 1892 successfully performed blood transfusion by rapidly drawing 20 c.c. of blood from the donor's vein, disconnecting the syringe, and emptying it through a needle placed in the recipient's vein before coagulation could take place. By filling the syringes one after the other, he was able to transfuse as much as 280 c.c. at one time.

Lindeman [16] in 1913 improved the technic by the addition of a large number of syringes, which were kept constantly washed by an assistant, and by devising a special nest of three cannulas, the outer one of which was rounded on its end to prevent injury to the intima. For a complete description of this method see page 100. It is cumbersome and requires a skillful team of workers, and blood clotting is an ever present danger. The principal historical importance of this method was that it furnished a stepping-stone to the

invention by Unger, two years later, of a very simple syringe and two-way stop-cock instrument.

Citrate Anticoagulation. A most important advance was made by Hustin [15] of Belgium in 1914 when he described a new method for indirect blood transfusion, using a glucose and sodium citrate solution as an anticoagulant.

Previous attempts with anticoagulants had been unsuccessful. Defibrination had proved at best to be a very awkward procedure. Hirudin, leech extract, had been tried, but its toxicity furnished a serious objection.

Agote [16] performed the first transfusion in which citrated blood alone was used, on November 14, 1914, in Buenos Aires. The technic was perfected by Lewisohn [17] in 1915, and the dosage of sodium citrate added was so adjusted as to be efficient as an anticoagulant and at the same time non-toxic. The technic elaborated by Lewisohn is generally considered today to be the most appropriate for indirect blood transfusions in which anticoagulants are employed. This method is described in detail in Chapter VII (see p. 96). The simplicity of the citrate method at once placed blood transfusion at the disposal of a great field of workers; whereas the intrinsic technical difficulties of the earlier procedures had limited its application to a small group of surgeons who had acquired the requisite skill.

Syringe and Stop-Cock. A very important mechanical contribution was made by Unger [18] in 1915, whose machine utilizes the principle of a syringe and two-way stop-cock. Clotting is retarded by means of a continuous ether-spraying of the syringe, and the apparatus is flushed from time to time with a salt solution. Because of its simplicity and reliability, Unger's method at once gained wide popularity. It offers a ready means, easily learned, of transferring from the vein of the donor to that of the recipient a measured quantity of unmodified blood without imposing serious

hardships upon either donor or recipient. Unger's method is described in detail in Chapter VII (see p. 102).

A great number of syringe methods for the transfusion of blood by the vein-to-vein method embodying somewhat different mechanical principles have been described in the recent literature. Space does not permit of their enumeration.

Elimination of Chamber. The author [19] has recently devised an instrument for the vein-to-vein transfusion of unmodified blood designed to still further simplify the manipulation, to eliminate the chamber, and to obviate the possibility of a reflux of blood from the recipient to the donor. The machine consists essentially of two disks rotating one upon the other through an angle of 90°. The proximal disk is perforated to form a channel for communication with the syringe; this opening alternately becomes continuous with either of two similar openings in the peripheral disk, for the inlet and outlet respectively. The writer's instrument and technic are described in detail in Chapter VIII (see p. 106).

There has been considerable controversy relative to the respective merits of the vein-to-vein syringe method and the citrate method of blood transfusion. As a matter of fact, both are methods of great value. The syringe method is the procedure of election; the citrate, that of expediency. Both have unquestionably established their worth.

The widespread use of the citrate method during the World War was largely responsible for the high regard in which the operation of blood transfusion is held today. The life-saving results observed from blood transfusions in hemorrhagic conditions incidental to military campaigns have made an indelible impression on the minds of physicians all over the world.

Present day technical methods are exceedingly satisfac-

tory and leave little to be desired. It is to be hoped that, in the near future, the medical mind will direct its attention to a more thorough crystallization of the indications for blood transfusion and to an extension of the field of usefulness of this therapeutic measure.

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CHAPTER II

Some Physiologic Considerations Relating to Blood Transfusion

Introduction. Physiology has necessarily been the forerunner and has paved the way for many of the outstanding contributions to medicine and surgery. In the case of blood transfusion, the reverse has to a considerable extent been true. Clinical observation has largely antedated physiologic investigation. Consequently, the technical procedures connected with the performance of blood transfusion have attained a considerable degree of perfection and the indications and contraindications for the operation have been fairly well defined. Our knowledge of the physiologic factors entering into the subject of blood transfusion, on the other hand, is still somewhat fragmentary.

Certain problems relating to blood transfusion are of sufficient importance to warrant separate consideration. Individual chapters have therefore been allotted to the blood groups (see p. 25), blood donors (see p. 44), the indications for blood transfusion (see p. 52), and untoward results from transfusion (see p. 77). The present chapter will embrace miscellaneous topics not included under these special heads.

Blood Coagulation. Blood clotting has always been one of the chief obstacles to the successful performance of transfusion. A brief exposition of the physiology of this subject is therefore in order.

Physiology. A few minutes after being allowed to flow

into a vessel, blood loses its fluidity and becomes viscous. It is soon converted into a soft jelly, which becomes firmer and firmer, until the containing vessel can be inverted without spilling the contents. Blood, on the average, starts to clot in from three to ten minutes, depending on such factors as the amount of blood drawn, the extent of the receiving surface, and the character of the containing vessel.

Clotting is due to the formation within the blood of a mesh-work of *fibrin.* The latter is an insoluble protein which is observed under the lower power of the microscope as a reticulum of fine threads. Under higher magnification, fine crystals can be made out. As this mesh-work shrinks, the clot becomes firmer. The red blood cells become entangled within the fine fibrin mesh-work, while the serum is expressed from the contracting clot. The great majority of the leukocytes are likewise caught in the mesh-work, although an occasional white blood cell may escape by virtue of its amœboid movement.

The process of coagulation begins with the disintegration of blood platelets, and probably also of leukocytes. The platelets, it has been shown, are derived from the megakaryocytes. The white blood cells shed forth into the plasma a substance called *prothrombin,* which immediately becomes activated and converted into *thrombin.* The thrombin reacts with a protein substance constantly present in the plasma, *fibrinogen,* as a result of which the insoluble protein fibrin is formed.

As to the nature of prothrombin and the character of the activating phenomena underlying its conversion into thrombin, there is much speculation. One established fact, however, stands out; namely, that the presence of the soluble calcium salts is essential to this change and that without calcium there is no coagulation.

Overcoming Coagulation. In the performance of blood

transfusion, the tendency to blood coagulation may be conquered in one of the four following ways:

(1) By rapidity of manipulation.

(2) By the reception of the blood through a strictly clean and smooth cannula, coated with a layer of paraffin or vaselin, into a vessel similarly coated.

(3) By defibrination.

(4) By the addition of anticoagulants.

Rapid Manipulation. The rapid transfer of blood from donor to recipient, before the blood has time to clot, is the principle employed by the various syringe methods. As cold retards coagulation, an ethyl chloride or ether spray thrown upon the syringe is a useful adjunct to this method. It is also important to bear in mind that the rougher the surface and the more extensive the area of surface contact, the greater will be the tendency to blood coagulation. In the choice of a particular syringe apparatus, therefore, a premium is placed upon three factors, with reference to the prevention of coagulation: namely, (1) ease of manipulation, (2) minimal surface contact area, and (3) continuous smooth surface.

Paraffin-Coated Vessels. Blood taken from a vein and transferred to a perfectly clean vessel may require from thirty to forty minutes before it jellies throughout. If the blood is allowed to come in contact only with surfaces which have been covered with a smooth layer of paraffin or vaselin, coagulation is delayed for a considerably longer period. This is the principle utilized by the Kimpton-Brown method of transfusion (see p. 94).

Defibrination. Blood clotting is caused by the formation of a mesh-work of fibrin. If, during the time of clotting, the blood is whipped vigorously with a bundle of fine rods, the latter will collect the fibrin as a stringy mass. The residual blood, called defibrinated blood, resembles normal blood in

appearance, but it cannot clot again. It consists of blood serum and corpuscles.

Bischoff's method of transfusion (see p. 5) utilized defibrinated blood, and many modifications of his procedure were long in vogue. All of the defibrinated blood methods of transfusion are now relics of the past.

Anticoagulants. The presence of calcium salts is indispensable to blood coagulation, and it has been shown that the removal of such salts prevents clotting. If freshly drawn blood is allowed to flow into an oxalate solution, it will remain unclotted for an indefinite period. If now a suitable amount of calcium salt is added, the blood will coagulate. The addition of the oxalate to the blood removes the calcium, which forms the insoluble salt calcium oxalate. Calcium, in some manner, plays an essential part in the first phase of coagulation, i.e., in the activation of prothrombin to thrombin.

Other anticoagulants whose action is similar to that of the oxalates are sodium fluoride and sodium citrate. The latter is of chief interest, in that it is extensively used for the performance of blood transfusion.

Sodium citrate on addition to blood forms with the calcium a soluble double salt in which the calcium is rendered inert. One hundred cubic centimeters of 2 per cent sodium citrate solution are sufficient to prevent coagulation on addition to 900 c.c. of freshly drawn blood.

Recently, Flandin and Tzanck [1] have recommended the use of arsphenamine instead of sodium citrate as the anticoagulant. They use sulpharsphenamine in the proportion of 0.03 gm. to 100 c.c. of blood.

There is another class of anticoagulants, which act not by interference with the calcium constituents of the blood but by directly preventing the reaction between fibrinogen and thrombin. These are the *antithrombins. Hirudin,* the

purified product of the salivary secretion of the leech, comes within this category.

Is Sodium Citrate Harmful to the Organism? The extensive use of citrated blood for transfusions renders this question one of supreme importance. It may be stated at the outset that the bulk of the evidence offers no justification for the opinion that the small amount of citrate thus administered entails any serious harm to the recipient.

Salant and Wise [2] in 1917, studying the manner of elimination of sodium citrate from the body, showed that nearly 90 per cent of the salt is thrown off within ten minutes after its intravenous injection. Most of it is destroyed by oxidation. The kidneys eliminate 30 to 40 per cent, the urine becoming alkaline during the process. Even when toxic doses were administered, there were no permanent ill effects.

Lewisohn, as a result of his experiments on man, asserted that as much as 5 gm. of sodium citrate in the form of a 0.2 per cent solution may be injected intravenously without harmful results.

Unger [3] has expressed the belief that the addition of sodium citrate to blood for transfusion gives rise to deleterious effects. He divided each specimen of blood from seventeen normal subjects into two equal portions. To one portion was added a 2 per cent solution of sodium citrate in the ratio used for a citrate transfusion; the other was not modified. From a comparison between the citrated and the unmodified bloods, Unger concluded that sodium citrate, even in the low percentages employed in transfusions, affects the red blood cells unfavorably, rendering them more fragile, diminishes the available quantity of complement, reduces the opsonic index almost to nil, and practically destroys the phagocytic power of the white cells.

On the contrary, Mellon, Hastings and Casey [4] repeated Unger's experiments but were unable to confirm any of his

findings. They failed to note any anticomplimentary action, except when the dose employed was so large that sufficient citrate was present to have this effect itself. They observed no increase in the fragility of the erythrocytes and no decrease in the phagocytic index of the leukocytes.

In experiments on exsanguinated dogs, Joannides and Cameron [5] proved that 0.2 per cent citrated blood is highly satisfactory as a transfusion medium, provided the amount of sodium citrate injected does not exceed 1 gm. They observed a prompt and pronounced rise in the blood pressure and a permanent improvement in the general condition of the animals. Their experiments prove that exsanguination does not increase the susceptibility of dogs to the effects of sodium citrate.

Clinical experience has shown that a definitely larger percentage of reactions occur after citrate than after transfusions with unmodified blood. This question will be discussed in Chapter VI (see p. 82). It cannot be justly stated, however, that the experimental laboratory has furnished us with any sound evidence constituting a serious objection to the addition of sodium citrate to blood for the purposes of transfusion.

Immediate Blood Changes after Transfusion. A study was made by Huck,[6] in twenty-one cases, of the blood changes immediately following transfusion by the citrate method. As a general rule, there was an immediate increase in the red cell count. In one case, this count rose from 180,000 to 1,488,000 immediately after the injection of 500 c.c. of citrated blood; in another it rose from 480,000 to 1,300,000 following the injection of 650 c.c. It is apparent that these striking alterations were due to a rapid redistribution of the transfused blood. However, the increase in the red cell count was not constant in this series. As a

general rule, there was also a definite rise in the hemoglobin and white blood cell count following the transfusions.

How Does Blood Transfusion Benefit? Blood transfusion accomplishes good in three chief ways, as follows:

1. It fills the vessels with a viscous medium.
2. It adds a considerable number of oxygen-carriers.
3. It furnishes a powerful hematopoietic stimulus.

In addition, there are unquestionably many other influences at work, dependent on the complex chemical nature of the blood. In the present state of our knowledge, any discussion of these lesser actions would be too speculative to be of any material value.

Restoration of Viscous Fluid. Surgical shock is accompanied by a state of depletion of the capillaries and smaller blood vessels. The latter exhibit an increased permeability, so that the injection of fluids of slight viscosity, such as isotonic salt solution, gives rise to no lasting benefit. The liquid is either passed in the urine or escapes from the vessels into the tissues. When solutions of gum arabic possessing approximately the same viscosity as blood are used, however, the tendency to permeation is largely overcome. The fluid is retained within the vascular tree and the results are much more favorable than when solutions containing only crystalloid bodies are injected. After the injection of acacia solutions, there is an early and sustained improvement in the pulse and a persistent elevation of the blood pressure. These observations would indicate that one of the factors accounting for the merit of transfused blood in the treatment of shock and hemorrhage is its viscosity.

Addition of Oxygen-Carriers. There is much experimental evidence in the field of physiology to prove the efficacy of blood transfusion in the treatment of states of exsanguination. Physiologists have established a standard hemorrhage in dogs, that is, a condition in which the dog is

as likely to live as to die. This standard hemorrhage is produced by systematically bleeding the dog until its blood pressure is 28 mm. When dogs with such a standard hemorrhage received sodium citrate solution intravenously, they died in every instance; when saline solution was injected, there was only temporary improvement. Results following injections of gum acacia solution were not much better. On the other hand, when compatible whole blood was transfused, all of the animals recovered.

One of the most noticeable results of a blood transfusion is an immediate improvement in color. This change is due to the addition of a large number of oxygen-carriers to the equipment of the recipient.

An illustrative example will help one to realize what a substantial boost is given to the oxygen-carrying capacity of the host by a blood transfusion. Take the hypothetical case of a woman weighing 130 lbs. Under normal conditions, her blood volume would probably occupy about 5 liters. Assume that as a result of a blood dyscrasia, her blood volume is reduced to 75 per cent of the normal and the red count to 40 per cent of the normal. In that case, her oxygen-carrying capacity, so far as the red blood cells are concerned, would be reduced to 30 per cent of the normal ($0.75 \times 0.40 = 0.30$), or to the equivalent of 1½ liters of normal blood. Under such conditions, the addition of 500 c.c. of blood from a healthy donor would constitute an increment of oxygen-carriers approximately equivalent to one-third the number already possessed by the recipient. In some severe cases of pernicious anemia, it is probable that a good-sized blood transfusion comes close to doubling the recipient's oxygen-carriers.

In view of the fact that the life of the red blood cell has been shown to be much longer than the short span of ten to twenty days, which was formerly believed to constitute

its period of existence (see p. 21), the increment of so relatively large a number of red blood cells would seem to account for a large share of the benefits accruing from blood transfusion.

Hematopoietic Influence. It has frequently been stated that much of the benefit derived from blood transfusion is attributable to the stimulation of the blood-forming organs by the donor's red blood cells, broken down soon after transfusion. This idea would appear to be erroneous, inasmuch as Ashby and others (see p. 21) have shown that there is no early disintegration of the donor's cells after transfusion. Whatever stimulation of the bone marrow occurs following transfusion is probably due to improved nutritional conditions in the bone marrow cells, brought about by the larger number of corpuscles in the blood. In this light, transfusion may be considered as acting in the rôle of a hematinic by breaking a vicious circle, rather than by directly stimulating the hematogenic areas.

In replacing the loss of the circulating medium of the body, nothing is equal to blood. Experiments on exsanguinated dogs have shown that such animals recover after transfusion of whole blood, whereas the controls receiving infusions of saline or acacia solutions perish in the great majority of instances. In man, clinical experience has shown that parallel results are the rule.

Absorption of Blood from Body Cavities. Many investigators have demonstrated that, in various animals, blood left in the peritoneal cavity is speedily absorbed. It has been shown that this absorption takes place through the thoracic duct in dogs. In these animals, blood may be detected in the thoracic lymph as early as eight and a half minutes after it has been injected into the peritoneal cavity.

Siperstein and Sansby[7, 8] in 1922 proved that citrated blood is rapidly absorbed from the peritoneal cavity of

rabbits, producing a sharp rise in the red cell count and the hemoglobin percentage. These experiments were confirmed and amplified by Ruh and McClelland.[9] When the easily identified nucleated erythrocytes of birds were injected intraperitoneally, these cells were found in the general circulation of the animals within fifteen minutes.

In experiments on twelve dogs, Opitz and Metis [10] found that foreign blood, whether defibrinated or citrated, is taken up by the circulation just as quickly as the animals' own blood. Furthermore, in additional experiments on thirteen infants, they showed that foreign red blood cells introduced intraperitoneally reappear in the blood stream.

It thus appears that after extensive intra-abdominal hemorrhages, a considerable portion of this extravasated blood is reabsorbed and utilized by the organism.

The Fate of the Transfused Red Blood Cells. Recent investigation has served to emphasize the importance to the recipient of the living transfused red blood cells. The part which these cells play in increasing the oxygen-carrying capacity has already been described (see p. 18).

The life of a red blood cell was formerly estimated at from ten to twenty days, but the data upon which this estimate was based have been shown to be somewhat inaccurate. The view that the erythrocyte has a life period of only ten to twenty days was originally based on the amount of bilirubin excreted per diem, but it has been shown that such estimations give only an approximate index to the amount of blood destruction.

Recent investigations have established the fact that the life of the red blood cell is much longer than was formerly believed to be the case. Ashby [11, 12] in 1919 reported the finding of transfused corpuscles in the blood of the recipient for periods extending over thirty days. When Group I (Janský) donors (universal donors) are used for

recipients whose bloods belong to Groups II, III, and IV respectively, it is possible to distinguish between the native and the foreign red blood cells in the blood of the recipient by treating the latter with a serum that agglutinates the recipient's cells. The donor's cells, on the other hand, are not agglutinated, as they contain no iso-agglutinable substance. All of the remaining unagglutinated cells after the addition of the agglutinating serum will represent erythrocytes originally obtained from the donor. Ashby found considerable numbers of such cells in the blood of various recipients for long periods of time. Her findings point to the conclusion that the beneficial results of transfusion are without doubt due primarily not to a stimulating effect on the bone marrow but to the functioning of the transfused blood corpuscles themselves.

Employing Ashby's method, Wearn, Warren and Ames [13] demonstrated that red blood corpuscles from donors of Group I (Janský), transfused into patients of Group II with pernicious anemia and anemia secondary to nephritis, remained in the circulation for from fifty-nine to 113 days, the average being eighty-three days. No difference was noted in the length of life of the transfused erythrocytes between recipients with primary and those with secondary anemia. Using a somewhat similar method, Jervell [14] demonstrated the presence of living transfused erythrocytes in an infant with melena neonatorum more than six weeks after the transfusion.

The fate of the transfused white blood cells is not known. Van der Hoff [15] found that, following blood transfusion, the white blood cell count may be increased, stationary or diminished. There is a tendency toward a relative increase of the polynuclears at the expense of the lymphocytes. In a case reported by Minot and Isaacs,[16] in which a patient with chronic lymphatic leukemia was used as the donor, the num-

ber and percentage of the recipient's lymphocytes fell to the pretransfusion level within two and a quarter hours, without any subsequent significant change.

Artificial Preservation of Red Blood Cells. That red blood cells artificially preserved are capable of functioning when transfused has been demonstrated. In Chapter VII (see p. 99) reference is made to Robertson's military method of performing transfusions with preserved cells. Kambe and Komiya[17] have submitted evidence to show that red blood cells, when preserved on ice for as long as twenty days, retain their vitality when transfused. If they are preserved in mixtures of isotonic sodium citrate and isotonic dextrose, they remain active for as long as thirty days.

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[8] *Ibid.*: Intraperitoneal transfusion with citrated blood. An experimental study. Am. J. Dis. Child., 25:107, 1923.

[9] Ruh, H. O. and McClelland, J. E.: Intraperitoneal transfusion in infants. Ohio State M. J., 19:780, 1923.

[10] Opitz, H. and Metis, F.: Zur Frage der intraperitonealen Blutinfusion. Jahrb. f. Kinderh., 107:269, 1924.

[11] Ashby, W.: The determination of the length of life of transfused blood corpuscles in man. J. Exper. Med., 29:267, 1919.

[12] *Ibid.*: The present status of the question of the length of life of the unagglutinable transfused red blood corpuscle. Arch. Int. Med., 34; 481, 1924.

[13] Wearn, J. T., Warren S. and Ames, O.: The length of life of transfused erythrocytes in patients with primary and secondary anemia. Arch. Int. Med., 29:527, 1922.

[14] Jervell, F.: Untersuchungen über die Lebensdauer der transfundierten roten Blutkörperchen beim Menschen. Acta Pathologica et Microbiologica Scandinavica, 1:201, 1924.

[15] Van der Hoff, H. L. M.: Het witte bloedbeeld gedurende de eerste uren na bloedtransfusie. Nederl. Tydschr. v. Geneesk., 67:571, 1923.

[16] Minot, G. R. and Isaacs, R.: Transfusion of lymphocytes: Their rapid disappearance from the peripheral circulation of man. J. A. M. A., 84:1713, 1925.

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CHAPTER III

Blood Groups

Introduction. If the serum of one animal is mixed with the red blood cells of an animal of another species, massive clumping of these cells may occur. This phenomenon is attributable to the interaction of a specific agglutinable substance in the red cells and of a corresponding agglutinating material in the serum.

A similar massive clumping of the red blood cells is observed in man when bloods from two incompatible individuals are mixed. *Iso-agglutination* is the term given to this phenomenon, as referring to the interaction between the cells and serum, respectively, of two individuals of the same species. For a description of the clinical phenomena resulting from massive iso-agglutination of the blood, see page 77.

Prior to 1900, nothing was known of the causes of blood incompatibility, except that violent reactions frequently followed the transfusion of blood. In that year, Landsteiner demonstrated the existence of two iso-agglutinins in serum and of two iso-agglutinable substances in the red blood cells. Later, on the basis of the varied combinations of these two pairs of substances found in the blood, it was possible to divide bloods into four groups and to show that only those belonging to the same group are compatible one with the other.

It is of interest to mention that blood group compatibility is also of importance in the selection of a donor for skin-grafting.

Jansky's Classification of Blood Groups Given Preference to That of Moss. The classification of the blood groups followed in this book is that of Jansky. In designating the groups, Group I by Jansky's classification becomes Moss' Group IV, and *vice versa*, while Groups II and III remain the same in the two classifications. Although the Moss scheme of grouping has somewhat the greater vogue, Jansky's work antedated it by three years and should there-

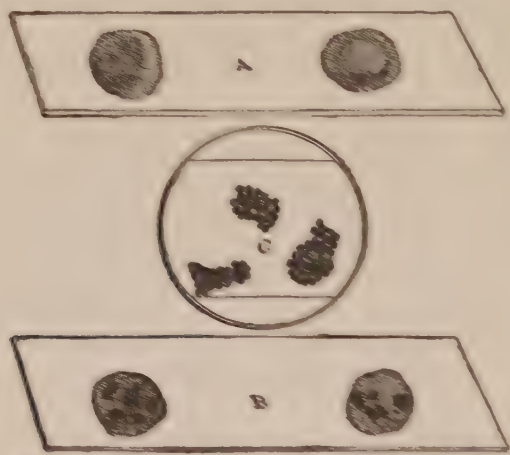

Figure 1. Determining blood group. A, non-agglutination. B, agglutination, microscopic. C, agglutination, microscopic, low power. (Fowler and Eggerth, Clinical Laboratory Medicine, published by Wm. Wood & Co.)

fore be given priority. Furthermore, in the interests of uniformity, a committee of the American Medical Association[2] has recommended the Jansky classification for universal use.

Much confusion would be avoided by designating the blood groups according to their content of iso-agglutinin and of iso-agglutinogen, as AB, Ab, aB and ab. In view of the fact that Guthrie and his collaborators have demonstrated the occasional presence of two additional iso-agglutinins and iso-agglutinogens and have furnished grounds for the

suspicion that still others exist (see p. 39), it is probable that the present schemata of blood grouping will have to be revised at an early date.

With respect to the alphabetical designations of the agglutinins and agglutinogens, there is lack of uniformity in the literature as to the use of the capital for the agglutinin or for the agglutinogen. For example, some authors speak of agglutinin *a* and agglutinogen A; others, of agglutinin A and agglutinogen *a*. Landsteiner used the capital letters for the agglutinogens. However, many important American communications, including those of Huck, Guthrie, and Pessel from Johns Hopkins Hospital, refer to the agglutinins as A and B, etc.; to the agglutinogens, as *a* and *b*, etc. This is the nomenclature that is followed in this book.

DESIGNATIONS OF THE FOUR MAJOR BLOOD GROUPS ACCORDING TO THREE CLASSIFICATIONS

Jansky	*Moss*	*Iso-agglutinin-agglutinogen content*
I	IV	AB
II	II	Ab
III	III	aB
IV	I	ab

Blood Groups. The great majority of human bloods may be divided into four groups according to their behavior when they are mixed with bloods from other individuals. Bloods from individuals of the same group mix without untoward phenomena; but, when incompatible samples are brought together, agglutination of the red blood cells, and sometimes hemolysis also, may occur.

Landsteiner's work established the fact that there are two iso-agglutinins in the serum, designated as iso-agglutinin A and B, and two iso-agglutinable substances resident in the erythrocytes, termed iso-agglutinogen *a* and *b*. Either iso-agglutinin causes clumping of the red cells in the pres-

ence of the homologous iso-agglutinogen. For example, a serum containing iso-agglutinin A will clump the red blood cells containing the iso-agglutinogen *a*, but no other cells. According to the possible combinations of the iso-agglutinins A and B and of the iso-agglutinogens *a* and *b* in blood, four groups may be distinguished as follows:

THE FOUR BLOOD GROUPS (JANSKY) ACCORDING TO CONTENT OF ISO-AGGLUTININ AND ISO-AGGLUTINOGEN

GROUP I	Plasma contains iso-agglutinins A and B. Corpuscles contain neither iso-agglutinogen.
GROUP II	Plasma contains iso-agglutinin A. Corpuscles contain iso-agglutinogen *b*.
GROUP III	Plasma contains iso-agglutinin B. Corpuscles contain iso-agglutinogen *a*.
GROUP IV	Plasma contains neither iso-agglutinin. Corpuscles contain iso-agglutinogens *a* and *b*.

Note: To transpose to the Moss classification, Groups I and IV are reversed, while Groups II and III remain the same in both groupings.

From a consideration of their content of iso-agglutinins and iso-agglutinogens, it becomes apparent that the following interactions will be observed between bloods of the respective groups:

INTERACTIONS BETWEEN BLOODS OF DIFFERENT GROUPS (JANSKÝ CLASSIFICATION)

Group I. Serum agglutinates corpuscles of Groups II, III and IV; corpuscles are agglutinated by no sera. This is the "universal donor" group.

Group II. Serum agglutinates corpuscles of Groups III and IV; corpuscles are agglutinated by sera of Groups I and III.

Group III. Serum agglutinates corpuscles of Groups II and IV; corpuscles are agglutinated by sera of Groups I and II.

Group IV. Serum agglutinates no corpuscles; corpuscles are agglutinated by sera of Groups I, II and III. This is the "universal recipient" group.

Note: To transpose to the Moss Classification, Groups I and IV are reversed, while Groups II and III remain the same in both groupings.

Inheritance of Iso-Agglutinin and Iso-Agglutinogen. The iso-agglutinogen content of blood has, as a rule, already been established at birth. This character has been shown to be a Mendelian inheritance (see p. 31). Either iso-agglutinogen, if present in one parent, may or may not be dominant in the offspring; but if a given iso-agglutinable substance is present in the child, it must of necessity be found in one of the parents. The medico-legal aspects of this problem are discussed on page 40.

The iso-agglutinins, on the other hand, are usually not formed until some months after birth. Once established, the individual's blood group does not change during his lifetime. A few apparent exceptions to this rule have been cited in subjects who have successfully withstood acute infections and in anemic patients who have recently been transfused. It would seem, however, that this apparent change in the blood group is really nothing more than a change in the titer of an iso-agglutinin constantly present but not recognized when of weak titer (see p. 34).

Iso-Hemolysis. In about 25 per cent of all subjects, iso-hemolysins are present in the blood in addition to the iso-agglutinins. When present, the substances responsible for iso-hemolysis follow the same groups as those which cause iso-agglutination, and they may therefore be disregarded for practical purposes.

Auto-Agglutination. Another phenomenon of theoretical interest is that of auto-agglutination. In rare instances, it has been found that cooling in the ice-box, sometimes even at room temperature, results in agglutination on mixing the corpuscles and serum of the same subject, which phenomenon does not occur at body temperature.

Frequency and Racial Variations of Blood Groups. Most of the observations upon blood groups have been made upon

Western peoples. The figures as to frequency given below are those of three separate American investigators.

FREQUENCY OF BLOOD GROUPS IN OCCIDENTAL PEOPLES
(JANSKÝ CLASSIFICATION)

Group	*Bernheim*	*Culpepper* (5000 tests)	*Moss* (1600 tests)
I	43%	41%	43%
II	40%	38%	40%
III	15%	18%	7%
IV	2%	3%	10%

Note: To transpose to the Moss classification, Groups I and IV are reversed, while Groups II and III remain the same in both groupings.

Most of the racial differences with reference to the relative frequency of the various blood groups occur in respect to Groups II and III. Among most European peoples, and of course Americans, the percentage incidence as regards these two groups is much higher in Group II. Group III, on the other hand, is the more common among Asiatic and African peoples. These racial differences are exemplified in the subjoined table:

INCIDENCE OF GROUPS II AND III IN VARIOUS RACES

	Group II	*Group III*
United States (mixed)	40%	7%
Malagasies	30%	28%
Negroes	27%	34%
Annamese	29%	35%
East Indians	27%	49%

For a more detailed study of this subject, the reader is referred to the very comprehensive report of Hirschfeld and Hirschfeld,[2] which was based on over 8,000 blood groupings made among the racially heterogeneous armed forces on the Macedonian front.

So long as they belong to the same blood groups, bloods from individuals belonging to different races are not incompatible. In their studies upon the various races in Egypt,

Dolbey and Mooro[3] found a perfect mutual agreement between the transfused bloods of Negro, Negro-Arab, Egyptian and Levantine races, and of fair-haired Turks or Circassians.

Blood Groups in Infancy. With regard to the conditions of blood compatibility found in infancy, many misstatements have been made. It has often been alleged that, in the case of an infant, the mother may safely be used as the donor without preliminary compatibility tests. Rapisardi and Pollitzer,[4] however, found that in seven out of twenty-five instances the mother's serum agglutinated the cells of her own offspring. Sometimes it has been stated that a baby has no blood group. This statement, also, is false. Reliance on the assumption that mother and child are necessarily compatible may lead to disaster under certain circumstances.

Blood groupings are hereditary and may be explained in terms of the Mendelian theory; but it by no means follows that the infant's blood group must be the same as that of its mother, or in fact of either parent. For a fuller discussion of this subject, see page 40.

As a general rule, the iso-agglutinogens are present at birth, while the iso-agglutinins are not developed until some months later. The blood of the newborn child, therefore, would be incapable of agglutinating the cells of another individual, no matter what his blood group. Furthermore, the blood from the parent-donor becomes so diluted by admixture with that of the recipient that the contained iso-agglutinins are usually so reduced in titer as to become ineffective.

While it is usually true that the serum of early infancy contains no iso-agglutinins, this is not always the case. Happ[5] has shown that at birth and during the first month of life the iso-agglutinins are rarely present but that the

percentage of infants in whom the blood group is established increases with age. After one year, the group is usually established; after two years, it is always present as in adults.

There are occasions, however, on which an infant may possess its final blood reactions very shortly after birth.

Such a baby must be treated in the same way as if it were an adult. Furthermore, even though iso-agglutinins are absent, the corpuscles of the infant may be so strongly agglutinophilic as to be clumped by the donor's iso-agglutinins, even though the titer of the latter is markedly diminished by dilution with the recipient's blood.

Another source of danger to be kept in mind is the fact that the effectiveness of iso-agglutinins is subject to great variation. It is possible, in exceptional instances, to obtain a blood whose iso-agglutinin titer is so exalted that, when used for donation, it would clump the cells of the recipient in spite of the gradual dilution incidental to transfusion (see p. 34).

Experience has shown that the likelihood of reactions from the transfusion of infants is much less than in adults. But from a consideration of all the possible dangers, it at once becomes apparent that the following rule is the only safe one to go by: *An infant prepared for blood transfusion must be subjected, as far as possible, to the same tests for group determination and blood matching as in the case of an adult.*

Method of Determining the Blood Group. For this purpose, sera known to belong to Groups II and III respectively are kept on hand. Agglutinating sera may be preserved in small glass capsules, the ends of which are sealed in the flame; such sera, if kept sterile, will remain active for months.

The use of dried sera for group determination is not to

be recommended. Karsner and Koeckert[6] have shown that, after drying, human iso-agglutinins deteriorate in two to three weeks and lose their group specificity in three to five weeks. Complete loss of specificity with coincidental acquisition of non-specific agglutinating power occurs in seven to ten weeks after desiccation.

Procedure. To about 5 c.c. of normal saline solution in a test tube add a drop of the patient's blood and shake so as to obtain a uniform suspension. Place a drop of known Group II serum and one of Group III serum upon opposite halves of a glass slide. To each of these drops of serum, add one drop of the corpuscular emulsion to be tested, mix well, and overlay with a coverglass. After one, five and ten minutes respectively, examine under the low power of the microscope. Agglutination is readily recognized by the fact that the red blood cells gather in dense, irregular clumps (see fig. 1). The latter are so large that they can often be seen with the unaided eye. When viewed over a sheet of white paper, they appear as brick-red granules. According to the behavior of the patient's blood with these two known sera, the blood group can be identified as follows:

Identification of Blood Group (Janský Classification)

Group I.	Agglutination occurs with neither Group II nor with Group III serum.
Group II.	Agglutination occurs with Group III but not with Group II serum.
Group III.	Agglutination occurs with Group II but not with Group III serum.
Group IV.	Agglutination occurs with both Group II and Group III serum.

After the patient and the donor have been typed and found to belong to the same group, the serum of the former is tested against the cells of the donor and the serum of the donor against the cells of the recipient. This

assures compatibility. In spite of this cross-matching, it is always wise to begin transfusions very slowly, as occasionally violent reactions occur even between two bloods of the same group. This subject is discussed more fully on page 39.

Sources of Error in Blood Matching. There are three principal sources of error in blood matching: namely, (1) rouleau formation, (2) variations in the titer of the iso-agglutinins and (3) the occasional presence of the rare iso-agglutinins or iso-agglutinogens.

Rouleau Formation. The presence of rouleau formation should not give rise to serious question. The rouleaux are very small, and, under the 4 mm. objective, the cells will be seen to lie in rows. Thorough mixing of the corpuscular emulsion and serum tends to avert rouleau formation and at the same time favors agglutination.

Variations in Iso-Agglutinin Titer. A very important source of error in group determination arises from the fact that the titer of the iso-agglutinins varies considerably in different individuals and may even vary in the same subject from time to time. This is particularly true in the case of sera of Group III. From this fact arises the necessity of matching the bloods before each transfusion, even though it may have previously been determined that the bloods are compatible. Without this precaution, there will be an occasional catastrophe.

If only the direct matching of bloods is performed, without determining the group, and if subsequently the same donor is used, there is always the danger of mixing incompatible bloods. One may happen to catch the donor at a time when the iso-agglutinin titer of his serum is so low as to be unable to clump the recipient's red cells even in the presence of the homologous iso-agglutinogen. Subsequently the titer of the prospective donor's iso-agglutinin

may be greatly enhanced, and, under these circumstances, massive agglutination of the recipient's cells may occur. Even in Group I, the so-called universal donor group, the iso-agglutinins may acquire such a high titer as to be able to clump the recipient's cells, notwithstanding the dilution of the iso-agglutinins resulting from the admixture of bloods (see p. 37).

It has been shown by Astrowe [7] that, in some instances, the iso-hemolysins and iso-agglutinins present in the recipient's blood may be greatly strengthened by a single blood transfusion in cases in which the injected blood, though compatible by direct matching, belongs to a different blood group. He cites the case of a girl eighteen months old, who received 180 c.c. of citrated blood from her mother with no reaction but who, twenty days later, after the transfusion of 130 c.c. from the same source, developed a violent reaction with hemoglobinemia. The blood of the child and mother, which had been shown to be compatible by direct matching prior to the first transfusion, was subsequently proved to have become incompatible. The mother's blood belonged to Group II (Janský); the child's, to Group I.

Other cases have been reported in the literature which would substantiate the view that blood transfusions may affect the titer of the recipient's iso-agglutinins and iso-hemolysins. Lindeman [8] and Thalheimer [9] have reported such cases. Pepper and Nisbet [10] reported a fatality with extreme hemolysis after the direct transfusion of blood by arterio-venous anastomosis. This was a second donation and the blood groups had not been determined. After the first transfusion there had been slight hemoglobinuria.

It should be noted, on the other hand, that following successive transfusions of 5 c.c. portions of blood in fifteen

different individuals, Mino[11] was unable to observe any changes in the iso-agglutinating properties of the recipients' blood. Variations in the iso-agglutinating titer of the serum such as occurred in the cases reported by Astrowe, Lindeman and Thalheimer are probably uncommon; nevertheless, one must constantly be on guard against them.

Such accidents as noted above serve to emphasize the fact that once compatible does not mean always compatible, *unless the donor and recipient both belong to the same group.* The determination of the blood group of donor and recipient should never be omitted; and certainly if reliance is to be placed on direct matching tests alone, a hazardous procedure at best, it is absolutely necessary to repeat these tests before each donation.

Diet is known to influence the iso-agglutinin titer of blood. Harper and Byron[12] have shown that a diet rich in greens increases the agglutinating power of the serum, while a green-free diet has the reverse effect. No change of group, however, is brought about.

The report that prolonged etherization brings about a change in the iso-agglutinative phenomena has not been substantiated. On the contrary, Huck and Peyton[13] found no change in the blood groups after ether anesthesia. Transfusions can be safely performed within twenty-four hours of prolonged ether anesthesia, provided a suitable donor has been found prior to the operation.

The Universal Donor. The corpuscles of Janský's Group I (Group IV according to the Moss classification) contain neither iso-agglutinogen *a* nor *b* and are therefore not agglutinated by the sera of the other three groups. Group I bloods, however, contain both iso-agglutinin A and B. Theoretically, therefore, blood from a donor belonging to Group I should agglutinate the erythrocytes of recipients

belonging to the other three groups. As a matter of fact, however, this occurrence is rare. In order to be effective the iso-agglutinins must be present in sufficient concentration. If the donor's blood is introduced very slowly, the titer of its contained iso-agglutinins is so reduced by dilution with the recipient's blood as to render them ineffective. For this reason, Group I has been called the "universal donor," meaning that, when a donor belonging to the same group as the prospective recipient cannot be found, Group I blood may be used for any of the groups.

Dangerous Universal Donors. The applicability of the term "universal donor" to Group I blood is only relative. In exceptional instances, the use of a universal donor may be highly dangerous. The routine direct matching of the bloods of prospective donor and recipient is necessary in order to detect these unusual cases. Dyke [14] has shown that the serum of Group I (Janský) subjects may vary in iso-agglutinative strength, not only in different persons but also in the same person at different times.

Levine and Mabee [15] have reported a case in which the blood of a prospective donor belonging to Group I exhibited remarkably strong agglutinating power. The titer of the iso-agglutinins contained in the blood of this "universal donor" was so high that 250 c.c. of his blood transfused into an individual belonging to another blood group would probably have resulted in massive agglutination of the recipient's red blood cells and perhaps death.

Another possible danger arising from the use of the blood of a universal donor is the occasional presence, in bloods coming within the classification of Janský's Group I, of the minor iso-agglutinins and iso-agglutinogens (other than A and B and *a* and *b*). Two of these pairs, namely iso-agglutinins D and Q and iso-agglutinogens *d* and *q*, have already been identified (see p. 39).

In view of the dangers mentioned above, I am of the opinion that the universal donor should never be used for a different blood group when by any possibility a donor of the same group can be found. Under exceptional circumstances, as when a patient in a very small community is found to belong to the relatively uncommon Group III or IV, it may be found extremely difficult to obtain a donor of the same group. In such emergencies, the use of the universal donor is permissible, but only after a most careful direct matching of the bloods of prospective donor and recipient. This direct matching of the bloods must be repeated with each subsequent transfusion from the same donor, because of the dangers arising from the variations in the titer of the iso-agglutinins (see p. 34). When a universal donor is used, the blood should be transfused very slowly, in order that the donor's iso-agglutinins may never be present in high titer in the recipient's blood. At the first sign of distress on the part of the patient, the transfusion should immediately be discontinued.

The Universal Recipient. The serum of Jansky's Group IV (Group I according to the Moss classification) contains neither iso-agglutinin A nor B and therefore agglutinates none of the cells of the other three groups. Group IV bloods, on the other hand, contain both iso-agglutinogens *a* and *b*. Group IV has therefore received the term "universal recipient," implying that in emergencies such individuals may with *relative* safety receive blood from donors belonging to any of the groups. It is assumed that the dilution of the donor's blood incidental to the transfusion so reduces the strength of his iso-agglutinins as to render them ineffective. But if, as sometimes occurs, the donor's iso-agglutinins should possess an unusually high titer, they will remain effective even after this dilution and massive

agglutination of the recipient's red blood cells will result. Furthermore, Dyke[14] has shown that the agglutinability of the corpuscles of different persons belonging to Group IV (Janský) exhibits considerable variation when matched with sera of Groups I, II and III. Quantitatively, all of the iso-agglutination phenomena appear to be a function of two variables, i.e., iso-agglutinin titer and relative iso-agglutinability.

It is evident, therefore, that individuals belonging to Group IV cannot be used as "universal recipients" with impunity. Whenever possible, a donor belonging to the same blood group should be selected. If circumstances compel one to rely on the principle of the "universal recipient," i.e., if the patient belongs to Group IV and a donor of the same group cannot be obtained, the bloods of donor and recipient must be directly matched, and this direct matching must be repeated before each subsequent transfusion. Furthermore, the transfusion must be given very slowly and discontinued at the first sign of distress on the part of the patient.

The Existence of Other than the Four Major Blood Groups. The division of bloods into four groups is based on the original supposition that there are only two iso-agglutinins and two iso-agglutinable substances present in blood. This assumption has been shown to be incomplete. Guthrie and Huck[16] in 1923, by direct tests and absorption experiments, demonstrated the existence of a third iso-agglutinin and of a third iso-agglutinogen. Their findings have an important bearing on the practice of transfusion and furnish a plausible explanation for some of the hitherto unexplained post-transfusion reactions. With these three iso-agglutinins and iso-agglutinogens twenty-seven biologic combinations are possible, and Guthrie and

his co-workers have already identified eight. Only bloods of the same iso-agglutinin and iso-agglutinogen content should be considered as belonging to the same group.

It will probably soon be necessary to revise the entire system of grouping bloods (see p. 26), and there is no more reasonable method of designating the different groups than by their content of iso-agglutinating and iso-agglutinable substances.

By their extensive studies, Guthrie and Pessel [17, 18] have so far identified two agglutinating and two agglutinable substances in blood, other than the major pairs Aa and Bb. The new iso-agglutinins are designated as D and Q respectively, and their homologous iso-agglutinogens as *d* and *q*. Guthrie and his collaborators suspect that other agglutinating substances may later be found. This whole subject is now in a state of flux.

Medico-Legal Applications of Blood Grouping: Determination of Paternity. The tendencies responsible for the different iso-agglutinative phenomena are hereditary and have been shown to descend in accordance with Mendel's law. Von Dungern and Hirschfeld[19] in 1910 studied the blood groupings of 348 persons belonging to seventy-two different families and thus established the fact that the iso-agglutinable substances present in the red blood cells are transmitted strictly in accordance with Mendelian laws. When either iso-agglutinogen *a* or *b* is present in both parents, it is found in most of the children; when it is present in only one parent, some of the children inherit it; when it is found in neither parent, no child ever inherits it. From the medico-legal point of view, then, if either iso-agglutinogen is present in the blood of the child, one of the alleged parents must necessarily possess it.

Ottenberg [20, 21] has devised some tables which would indi-

cate that the study of the blood groups promises to be of considerable help in deciding questions of disputed paternity. A detailed analysis of the offspring resulting from unions of persons belonging to various groups shows that in certain instances the possible blood groups of the offspring are sharply limited.

LIMITATION OF OFFSPRING (OTTENBERG)

Unions of I and I give only I

Unions of I and II
Unions of II and II give only I and II

Unions of I and III
Unions of III and III give only I and III

If the child's blood is in the correct group for the alleged parent (referring to group of limitation of offspring in the above table, not to the blood group), we can say that it may be their offspring, but is not necessarily so. But if the child's group is wrong for the two asserted parents, we can say positively that the child must have one parent other than the two alleged. This does not imply that the child must necessarily belong to the same blood group as either parent. Thus a union of two parents both belonging to Group III may result in a child belonging to Group I. On the other hand, if the child belongs to Group III or IV and one parent belongs to Group I and the other alleged parent to Group II, it is safe to state that that child is illegitimate, because it has inherited a specific iso-agglutinable substance, namely iso-agglutinogen *a*, not possessed by either of the alleged parents.

Ottenberg has formulated certain definite laws in connection with the blood group by means of which he contends that in certain instances the illegitimacy of children may be determined:

INSTANCES IN WHICH THE CHILD MUST BE ILLEGITIMATE, OR NOT THE CHILD OF THE SUPPOSED FATHER (OTTENBERG)

Known Mother	*Supposed father*	*Child*
I	I	II III IV
I	II	III IV
I	III	II IV
..	...	.....
II	I	III IV
II	II	III IV
...	...	.....
III	I	II IV
III	III	II IV
...	...	.....

PREDICTION OF REMAINING PARENT GROUP (OTTENBERG)

Known children in group	*One parent known to be in group*	*The other parent must be in group*
II	I	II or IV
II	III	II or IV
III	I	III or IV
III	II	III or IV
IV	I	IV
IV	II	III or IV
IV	III	II or IV
II and III	I	IV
II and III	II	III or IV
II and III	III	II or IV
II and IV	I	IV
II and IV	II	III or IV
II and IV	III	II or IV
III and IV	I	IV
III and IV	II	III or IV
III and IV	III	II or IV
II, III and IV	I	IV
II, III and IV	II	III or IV
II, III and IV	III	II or IV

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CHAPTER IV

Blood Donors

Introduction. The proper selection of a blood donor is obviously a matter of importance. A great deal of individual variation will be found among prospective donors. For the best results, it is necesary to make the choice only after a careful examination of the available candidates. In any case, the donor and the patient must belong to the same blood group and their bloods must be compatible by direct matching. This subject is discussed fully in Chapter III (see p. 25).

Choice of Donor. The principal factors to be taken into consideration in the selection of a blood donor may be classified under the following headings: (1) age, (2) sex, (3) general health, (4) hematologic status, (5) freedom from communicable disease, (6) blood group, (7) emotional status and (8) preëxistence of a particular infectious disease.

(1) *Age.* Vigorous young adults make the best donors. The military age, that is from eighteen to forty-five years, roughly expresses the age group from which a donor may be selected. If the patient is too young, his psychologic reaction may render him undesirable; if he is too old, there is always a danger of inadequate blood regeneration.

(2) *Sex.* It is more convenient to use men as donors, although women are more apt to volunteer. The larger and more accessible superficial veins and the less amount of subcutaneous fat simplify the technic when males are

used. Furthermore, Giffin and Haines[1] have noted that female donors recover their cell volume and hemoglobin more slowly and are apt to develop a slight but definite anemia. Of the women of their series, 65 per cent showed some slight hematologic defect following blood donation.

(3) *General Health.* The better the general health of the subject the more valuable will his transfused blood be. This statement sounds trite, but it must be admitted that its importance is often overlooked. When time permits and several donors are available, they should be examined in order to choose the most vigorous. The presence of any serious disease, of course, is sufficient to disqualify a prospective donor. The examiner should glance at the bend of the elbow to be sure that the superficial veins are reasonably accessible.

(4) *Hematologic Status.* The quality of the blood to be transfused is manifestly a subject of first importance, yet this aspect is sometimes neglected. It is certainly at least as important to know the quality of the blood which one is administering intravenously as to be assured that the drugs which one is prescribing are of the first quality. This knowledge requires a minimum of a red cell count and a hemoglobin reading.

Among professional donors, a preliminary hematologic survey is especially important. Some subjects who offer their blood reveal a more marked anemia than the patients to be transfused. Famulener[2] found twenty professional donors with a hemoglobin content below 85 per cent. The lowest reading which he observed was 57 per cent of hemoglobin with a red cell count of 2,000,000.

I have had under my observation three very anemic professional donors with hemoglobin readings of 30, 40 and 70 per cent, respectively. In one of these subjects retinal hemorrhages were present.

(5) *Freedom from Communicable Disease.* Syphilis, malaria, and measles are the principal infectious diseases which may be transferred by blood transfusion. The transmission of bronchial asthma with allergy to horse dandruff by this means has been reported. The subject of the communication of disease through blood transfusion is taken up in greater detail in Chapter VI (see p. 86).

Except in emergencies, the Wassermann test should invariably be performed and the blood smear should be searched carefully for malarial organisms. The history, likewise, should be investigated with reference to syphilis and malaria. Other diseases characterized by the presence of parasites in the blood-stream may likewise be transmitted by blood transfusion. With reasonable precautions, the danger of transmitting infection by this means should be slight.

(6) *Blood Group.* The donor and the patient should belong to the same blood group, except in the unavoidable instances in which the universal donor or the universal recipient must be employed. This subject is discussed at length in Chapter III (see pp. 36-39).

(7) *Emotional Status.* The high-strung temperamental subject does not make a good donor. In the first place, his behavior during the operation is likely to interfere with the smoothness of the procedure. Furthermore, such a patient is too apt to be overimpressed with his self-sacrifice and to develop a hero complex, as we might term it.

The neurotic patient who has parted with a pint of blood is quick to ascribe all of his symptoms, both real and imaginary, to that source. For his own peace of mind, if for no other reason, the operator will do well to avoid donors of the emotional type.

(8) *Preëxistence of Particular Infectious Disease.* In treating a patient for some specific infectious disease by

means of blood transfusion, it is often advisable to employ as the donor an individual who has recovered from the same condition. In the case of measles, the blood of a subject who has recovered from an attack of the disease is remarkably beneficial (see p. 70). A similar specific protective property is probably present in the blood of persons who have recovered from scarlet-fever, poliomyelitis and certain other infectious diseases.

Professional Donors. In most of the larger cities of the United States professional donors are now available. Professional donorism has to some extent arisen as a response to advertisements appearing in the newspapers from time to time offering rewards for blood. Professional donors have even organized agencies and have standardized their fees.

The organization, reliability and predetermined blood grouping of professional donors make for efficiency and convenience, especially in emergencies. Professional donors know exactly what is expected of them and are not troubled with the heroic attitude which quite naturally accompanies the unpaid giving of blood.

When it is possible to obtain a healthy compatible donor in the family, I advocate that he be given the preference. When a good family donor cannot be procured, I believe that the professional donor should be our second choice. I am not in favor of indiscriminate voluntary donorism, and I do not approve of the practice of having students or hospital internes give up their blood.

Harmlessness of Blood Donation. It might be thought that the often repeated donations of blood required of professional donors might eventually lead to an anemia, but such does not appear to be the rule. Following the loss of 500 c.c. or even more of his blood, the average individual experiences practically no discomfort. As a matter of fact,

the majority of donors seem to feel somewhat better a few days after the donation and there seems to be a tendency toward a slight gain in weight. It takes a normal man on an average of three weeks to recover from the loss of one pint of blood. It would thus appear that the common therapeutic bleedings practiced during bygone centuries were justified, at least to the extent that they caused no harm.

Giffin and Haines [1] studied an unselected group of eighty-four professional donors and observed no harmful results after multiple donations of 500 c.c. given at intervals of four to five weeks. Women, however, recuperated more slowly than men (see p. 45).

The author has observed a professional donor who submitted to fifty-nine donations of blood within a period of nineteen months. The maximum loss at any time was 800 c.c. The total amount of blood given during the period was 23,960 c.c. The subject is still in perfect health and has exhibited no demonstrable disturbance from his multiple blood donations. His hemoglobin reading, however, is only 70 per cent.

On the other hand, I have observed three professional donors who developed rather severe anemias, apparently from their donations (see p. 45).

Cardiovascular Reactions. A careful study of the immediate cardiovascular reactions following blood donations was made by Eyster and Middleton.[3] These workers studied the diastolic silhouette area of the heart by means of the Roentgen ray in subjects who had just submitted to donations of 500 c.c. of blood, that is about 10 per cent of their total volume. They noted that the immediate reduction in the outline of the heart was very slight and that in all cases the transverse diameter had returned to within 2 per cent of the normal within one hour of the donation.

As a rule, there was rather a sharp fall in the systolic, diastolic and pulse pressure immediately after the bleeding; all of these figures rapidly returned to approximately normal readings.

The recipients, likewise, showed no morbid changes in the cardiac silhouette. They usually exhibited a transitory rise of blood pressure.

The Universal Donor. Individuals belonging to Janský's Group I are known as universal donors. Their blood contains neither iso-agglutinogen *a* nor *b* and is therefore not agglutinated by the sera of the other three groups. I believe that the applicability of the term "universal donor" is only relative and that, in exceptional instances, the use of a Group I donor for individuals belonging to other blood groups may result disastrously. This subject is discussed in detail on page 36.

Immunized Donors. The conception that by a preliminary period of vaccination of the prospective donor with the organism isolated from the patient the bactericidal power of the donor's blood may be considerably enhanced and may thus materially assist the recipient to overcome his infection, has a *prima facie* appearance of merit. It cannot be said, however, that striking results have been obtained by this method. The most that can be claimed is that the method is still in the experimental stage, and that there is a possibility that it may be found to be of value. Transfusion of blood from the immunized donor has been tried with indifferent results in subacute bacterial endocarditis.

The vaccination of the prospective donor follows the usual procedure employed in vaccine therapy. With most bacteria the initial dose should be about one hundred million killed organisms given subcutaneously. The increments of dosage and the intervals are gauged according to

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clinical indication, care being taken to avoid an injection during the negative phase. As a general rule, an interval of from four to seven days will be found best. The titer of the immune bodies in the donor's serum should be determined before using his blood for transfusion and the transfusion should be given at a time when the phagocytic index is high.

Alkalinized Donors. The high content of alkaline buffers and the oxygen-carrying capacity of blood would suggest the value of transfusion in acidotic states. In this connection, an attempt has been made to increase the alkaline buffers of the blood of the donor prior to transfusion. Gettler and Lindeman[4] reported a case of hyperemesis gravidarum with laboratory evidences of acidosis in which the transfusion of 400 c.c. of blood from a donor previously alkalinized resulted in an instantaneous change for the better and ultimate recovery. The donor in this case was treated for sixteen hours prior to giving his blood with 20 gm. of sodium bicarbonate every two hours.

Accidents to Donors. With modern technic, serious accidents to donors are very rare. Some donors, of course, faint; but this symptom is due to the sight of the blood, not to its loss. For a day or so after a large donation, there may be a certain amount of giddiness, but this symptom is only transient.

At the same time, it must be admitted that there is a possibility of transmitting disease from the patient to the donor when some of the modern syringe methods are employed. Many of these instruments, especially those of the ball-valve type, are not proof against a reflux of blood from the recipient to the donor. Instances in which infection of the donor has thus taken place are probably rare, but they have undoubtedly occurred. That they do not

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take place more frequently is probably to be credited to the high powers of resistance of the average donor.

Elimination of Reflux. It was for the purpose of obviating the possibility of a reflux of blood from patient to donor as well as of simplifying the instrumental manipulation that the author[5] conceived and devised his simple blood transfusion apparatus (see p. 106).

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CHAPTER V

Indications for Blood Transfusion

Introduction. It is only since 1914 that both simple and safe methods of performing blood transfusion have been available. Before that time the operation was considered largely as an emergency procedure to be performed only by those possessed of special skill and training. Nevertheless a considerable mass of data relative to the therapeutic indications for blood transfusion has been collected within recent years, especially during the period of the last decade.

Certain pathologic conditions stand out as paramount indications for the performance of blood transfusion. At the same time, it must not be thought that because definite groups of abnormal states are tabulated the whole field has been explored. Such is far from the truth. New facts are constantly brought to light which would indicate that there is still a great deal to be learned concerning the therapeutic possibilities of blood transfusion.

Enumeration of Indications for Blood Transfusion. The indications for blood transfusion may be enumerated as follows:

1. Sudden losses of blood from any cause.
2. Surgical shock.
3. Illuminating gas poisoning.
4. Chronic hemorrhagic diseases of the blood.
5. As a preoperative precaution when the bleeding and clotting time has been found to be delayed.
6. Blood dyscrasias.

7. Subacute systemic bacterial infections.
8. Acute septic conditions.
9. Diabetic coma.
10. Debilitated conditions.
11. Miscellaneous indications.

(1) Sudden Losses of Blood. To check hemorrhage was one of the earliest uses for which blood transfusion was employed, and perhaps the most brilliant results are obtained in this group of cases. The transfusion not only replaces the blood loss and furnishes an immediately available supply of oxygen-carriers, but it also constitutes the most efficient means of checking the bleeding. In the majority of cases of acute hemorrhage a single transfusion is sufficient to accomplish this purpose.

So far as the control of the hemorrhage is concerned, blood transfusion appears to be uniformly beneficial no matter what the origin of the bleeding. Of course it does not always save life, as the prognosis is conditioned by the disease which gives rise to the hemorrhage.

Obstetric Emergencies. The hemorrhagic emergencies of obstetric practice, such as ruptured ectopic gestation, placenta previa, premature separation of the placenta and postpartum hemorrhage, are prime indications for blood transfusion. As a preoperative or postoperative measure, blood transfusion is frequently life-saving.

I have records of two cases of extrauterine pregnancy with rupture and collapse. Both patients recovered, and in each instance the transfusion was followed by immediate improvement and was undoubtedly the important factor leading to the favorable result. In a case of placenta previa with continuous bleeding and in one of premature separation of the placenta in which the patient was almost exsanguinated, blood transfusion stopped the bleeding immediately. Both of these patients recovered. Likewise, in

two cases of fibrosis uteri in which blood transfusion was employed as a preliminary to radium treatment, hemorrhage was stopped and the outcome was favorable. In incomplete abortion, a blood transfusion prior to operation has, in my experience, proved a valuable adjunct. For the employment of blood transfusion in puerperal sepsis see page 69.

The routine group determination and matching of all prospective mothers and the selection of a donor beforehand, to be used if needed, are recommended. A plan has been suggested by Titus,[1] whereby every obstetric patient, within six to eight weeks of her expected delivery, has her blood matched with that of her husband and four other persons who might be used as donors in case of emergency.

Other Hemorrhages. Losses of blood arising from gastric or duodenal ulcers or from the rupture of an esophageal varix in cirrhosis of the liver show the same striking benefit from transfusion. Of three of my patients with very severe hemorrhages from a gastric ulcer, two immediately stopped bleeding and recovered after transfusion. One of these patients, a man twenty-five years old, was semiconscious and pulseless. After the administration of 600 c.c. of blood he had no more hemorrhage and made a good recovery. I had a similar favorable experience in one case of duodenal ulcer, also in a case in which there was persistent bleeding from an ulcerated colon.

In typhoid fever, with hemorrhage from the intestine, blood transfusion is likewise an important means of checking the bleeding. As soon as blood is detected in the stools, preparations should be made for the performance of a transfusion at short notice. In dysentery, the patient's general condition and the bleeding tendency are undoubtedly improved, although the local process does not appear to be affected.

(2) **Surgical Shock.** Blood transfusion is unquestionably of great value in the treatment of surgical shock, provided that it is given early. Crile's early experiments on dogs showed that under carefully controlled conditions blood transfusion may be life-saving. Clinical experience has, to a degree, paralleled the results of his experiments. The all important desideratum, however, is that the blood transfusion must be given early, that is, within a few hours of the onset of shock. When a long period of time is allowed to elapse before the transfusion is given, irreparable damage to the vital centers is apt to occur.

Surgical shock has been shown to be associated with a very low systolic blood pressure and with dilatation and increased permeability of the peripheral capillaries. Owing to the escape of fluid through the walls of the capillaries, there is a poverty of blood within the heart and vessels. Measures to refill the vascular tree are obviously in order, and intravenous infusions of normal saline solution have been extensively employed for this purpose. Because of the increased permeability of the capillaries, however, this fluid is soon lost into the tissues. Some of it is also passed in the urine. Having in mind this experience, Bayliss during the World War employed a 6 per cent solution of gum acacia with 0.9 per cent sodium chloride. It was reasoned that, because of its viscosity, this solution would be retained within the blood vessels. Statistical studies have shown that in surgical shock the results obtained with gum acacia solution are superior to those following the use of normal saline, but certainly not to be compared with those obtained after blood transfusion.

Obviously, blood itself is a liquid of just the proper viscosity and it possesses the additional great advantage of supplying an immediate increment of oxygen-carriers. The general properties of fresh healthy blood in combating tox-

emia would further suggest that it might also be of value in overcoming the histamine toxemia which causes the shock. Furthermore, it has been shown that the imperfect oxygenation in the tissues associated with shock results in a shift of the pH toward the acid side. In that case, the addition of the normal alkaline buffers of blood would be expected to be of value.

Accumulated experiences during the World War as to the treatment by blood transfusion of shock resulting from gunshot wounds were most favorable. There is no question but that blood transfusion should be employed much more frequently than it now is for the prevention and treatment of surgical shock and that it should be given early, not as a last resort.

In debilitated patients, or when a very extensive surgical procedure is contemplated, a blood transfusion immediately before or after the operation would do much to lower the mortality.

(3) Illuminating Gas Poisoning. In poisoning with carbon monoxide, the hemoglobin of a large number of the red blood cells has combined with this gas. As carboxyhemoglobin is more stable than oxyhemoglobin, the affected cells are lost to the individual. It would therefore seem probable that blood transfusion, by replacing a number of these useless cells, would be of great value; that is, in a disease in which oxygen-carriers are lost the administration of fresh oxygen-carriers would seem logical. Experience has shown that such is the case.

Bermeister,[2] in 1916, in a series of experiments on rabbits and dogs poisoned with coal gas, showed that recovery took place in 75 per cent of the cases when the transfusion of preserved living erythrocytes was employed; whereas nearly all of the control animals died.

Robertson [3] reported two cases of severe carbon monoxide poisoning in man in which good results were obtained by simultaneously removing and transfusing one liter of blood. This procedure of exsanguination-transfusion is described in Chapter X (see p. 131).

The most efficient treatment for illuminating gas poisoning, however, is to place the patient in a specially constructed chamber where he can breathe oxygen under a pressure approximating three atmospheres. Under these conditions, the carbon monoxide is freed from its combination with hemoglobin. Such an apparatus, however, is seldom available.

Other Poisons. It is highly probable that blood transfusion will eventually prove valuable in the treatment of poisoning with other substances which, like carbon monoxide, have a deleterious effect upon the red blood cells. Hindse-Nielsen [4] reported a case of poisoning with nitrobenzol, which substance results in the formation of methemoglobin in the red blood cells. The patient was a girl, nineteen years old. Although her condition was apparently hopeless, she recovered after blood transfusion.

McClure [5] in 1916 reported a case of benzol poisoning with severe purpura hemorrhagica and anemia of the aplastic type which was successfully treated by blood transfusion. In a period of six weeks, five transfusions were given. The red blood cells were increased from 1,226,000 to 4,528,000 and the hemoglobin from 20 per cent to 65 per cent.

It would also appear that in cases of poisoning with hydrocyanic acid blood transfusion may be of value.

(4) Chronic Hemorrhagic Diseases of the Blood. Under this heading we shall discuss the employment of blood transfusion for the relief of the hemorrhagic tendencies associated with hemophilia, purpura hemorrhagica, jaun-

dice, melena neonatorum, and also pernicious anemia and the leukemias.

Hemophilia. In hemophilia blood transfusion acts as a specific, but only temporary, remedy. Whatever the causative factor, the outstanding feature in this disease has been shown to be a delay in the coagulation time of the blood. Many observations are recorded which are in accord to the effect that a single blood transfusion in a hemophiliac commonly results in a marked reduction of the clotting time, but that this effect soon passes away. Some of these observations are tabulated below:

Effect on Clotting Time of Single Blood Transfusion in Hemophilia

Coagulation Time in Minutes

Observer	*Before transfusion*	*Soon after transfusion*	*Highest subsequent*
Addis [6]	245	24	200
Bulger [7]	55	10	55
Minot and Lee [8]	150	8	115
Pemberton [9]	23	3	20

To control the bleeding in hemophilia, no remedy is superior to blood transfusion. When surgical procedures upon a hemophiliac are required, a blood transfusion should invariably precede the operation. It has been shown that the injection of even a small amount of blood is sufficient to stop bleeding. For hemostatic effect alone, the transfusion of 100 c.c. of blood is enough.

As the tendency to severe bleeding in hemophiliacs decreases with age, it would be a good plan to subject such individuals to periodic transfusions of small amounts of blood during their earlier years. It might be possible to tide them over the dangerous age by this means. At all events, when it has been determined that an individual is a hemophiliac, his blood group should be determined at

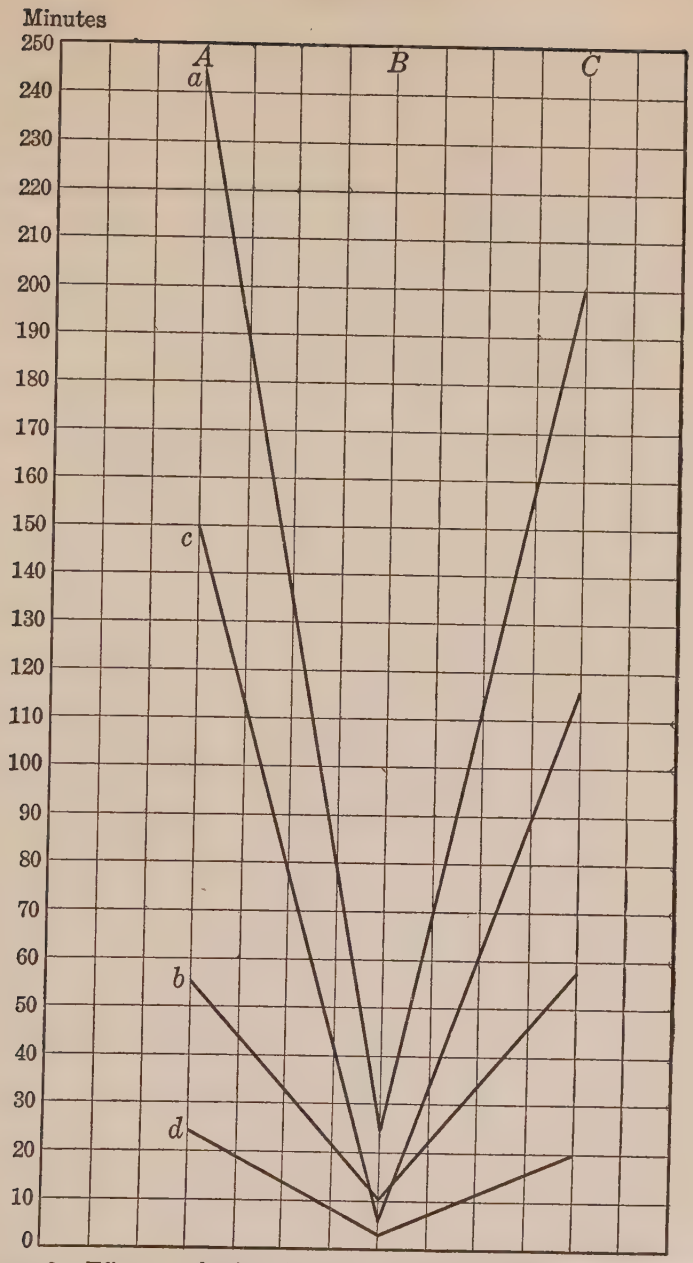

Figure 2. Effect on clotting time of a single blood transfusion in hemophilia according to four different observers. A, before transfusion; B, soon after transfusion; C, slowest subsequent clotting time. a, Addis; b, Bulger; c, Minot & Lee; d, Pemberton.

once, one or more donors selected in advance, and all of the persons concerned instructed as to what is expected of them in case of emergency.

There is no objection to the employment of the citrate method for blood transfusion in hemophiliacs. As a matter of fact, Ottenberg [10] has observed that the intravenous injection of sodium citrate actually reduces the coagulation time in hemophilia. In a hemophiliac whose clotting time was ninety-five minutes, the injection of 20 c.c. of a 3 per cent solution of sodium citrate reduced this period to twenty-five minutes. Forty-eight hours later, however, the coagulation time had been lengthened to 170 minutes.

Purpura Hemorrhagica. Opinions with regard to the efficacy of blood transfusion in the treatment of purpura hemorrhagica are somewhat conflicting. In a series of nine cases, Ottenberg and Libman [11] observed six complete recoveries and two deaths following blood transfusions. In their experience there was a prompt cessation of the bleeding in most of the cases. Unger,[12] on the contrary, remarks that the results of transfusion in purpura hemorrhagica are only fairly good and that repeated transfusions are often necessary to control the bleeding. Peterson [13] gave twelve transfusions to seven patients with purpura hemorrhagica. In three cases a single transfusion corrected the bleeding tendency and apparently cured the condition. In two other cases in which hemorrhage was active and life was threatened, the transfusion tided the patient over the emergency. The results of blood transfusion in the other two cases were not favorable and the patients died. Larrabee [14] reported three cases of purpura hemorrhagica, in two of which the bleeding tendency was controlled and the blood platelet count restored to normal by blood transfusions. In the third case, the bleeding likewise was controlled, after six

transfusions, and the platelet count was increased; but the patient died of a complicating gangrenous appendicitis.

I have treated two children with purpura hemorrhagica by means of blood transfusions. One of them, a girl seven years old, with very extensive purpuric skin lesions, recovered after two transfusions, her platelet count rising from 50,000 to normal. The other patient, a boy thirteen years old, showed no benefit from transfusions and died soon afterward. However, he was *in extremis* at the time the procedure was employed.

Jaundice. In the severer grades of jaundice the coagulation time of the blood may be greatly prolonged. It may be three or four times the normal. Blood transfusion diminishes the clotting time, but this effect soon passes away.

As an emergency measure to control hemorrhage or to lessen the risk from this source during an operation, transfusion is of value. Its effect, however, is transient, and, after a few days, bleeding is apt to recur.

Melena Neonatorum. In the severe hemorrhages which sometimes take place from the bowel of the newborn infant, a single blood transfusion is usually curative. Recoveries have been observed even in moribund patients. The amount of blood required is small, 15 c.c. for each kilogram of body weight serving as a good general rule (see p. 120).

Bleeding from other sources in the newborn is also checked to a remarkable extent by blood transfusion. Bleeding or oozing from the umbilical cord, hemorrhage as a result of circumcision and the bleeding associated with icterus neonatorum are all favorably influenced.

I have observed one case of icterus neonatorum, with a familial history of two deaths from the same cause. Transfusion in this case, however, yielded no benefit and the infant died.

Lewisohn[15] in 1918 reported eight cases of bleeding in infancy, six of which were cured by a single transfusion by the citrate method.

Because of the small size of the superficial veins, transfusion in infants presents difficulties. In Chapter IX (see p. 121) this technic is described.

Pernicious Anemia and the Leukemias. The effect of blood transfusion upon the morphology of the blood and the general condition of the patient in pernicious anemia and the leukemias is discussed elsewhere (see pp. 62-68). These diseases are commonly associated with hemorrhagic tendencies and for the relief of this bleeding blood transfusion is a useful measure. However, I have records of two fulminating cases of acute leukemia, one of the lymphatic and one of the splenomyelogenous type, in which blood transfusion failed to control the hemorrhage.

(5) Preoperative Precaution with Prolonged Bleeding and Clotting Time. This subject has already been discussed in connection with hemophilia and cholemia (see pp. 58-61). The tabulation on page 58 and also figure 2 show what a marked reduction in the coagulation time in hemophilia may be brought about by blood transfusion. The preoperative determination of the bleeding and clotting time is now pretty much of a routine. Experience has shown that a tendency to excessive bleeding during and after operation may, to a large degree, be controlled by preliminary blood transfusion.

(6) Blood Dyscrasias. Among the most remarkable of the results obtained from blood transfusion are those witnessed in pernicious anemia. The diseases discussed under this heading are pernicious anemia, the leukemias and the so-called secondary anemias.

Pernicious Anemia. In a disease characterized by a poverty of circulating erythrocytes, it would be expected that

an increment of red blood cells would give rise at least to a temporary improvement. As a matter of fact, not only are the immediate results beneficial but in more than half of the cases, repeated transfusions lead to a remission. The disease is not cured. Ottenberg and Libman [11] observed fourteen more or less prolonged remissions immediately following transfusion in a series of twenty-five cases of pernicious anemia thus treated. Anders [16] reviewed the literature of 362 cases of pernicious anemia treated by blood transfusions and noted that in 204, or 56.3 per cent, of these cases a remission was thereby initiated. The average number of transfusions per patient was 2.4.

The immediate improvement which follows blood transfusion in pernicious anemia is often striking. Scheel and Bang [17] reported a case of addisonian anemia in a man of thirty-three with a red blood cell count of 850,000 and 19 per cent hemoglobin. The patient was semiconscious and dyspneic and appeared ready to die. Following the transfusion of 900 c.c. of citrated blood, there was immediate improvement and the red blood cell count rose to 3,118,000. Twelve days later the patient was on his feet. Every observer can cite instances in which apparently the most hopeless cases of pernicious anemia have shown marked temporary improvement and prolongation of life as the result of blood transfusion.

The effect of blood transfusion upon the red blood cell count in pernicious anemia is remarkable. The count immediately following a transfusion is commonly doubled. It may be increased eightfold. This immediate increase is to be attributed to the direct addition of the donor's cells, also in part to a redistribution of the erythrocytes. It has been shown by Ashby (see p. 21) that these cells may circulate in the host for periods of a month or longer. Later, there may be a progressive improvement in the morphology

of the blood until it approximates normal. It is commonly stated that this improvement is brought about as the result of the stimulating effect of the donor's corpuscles upon the patient's blood-forming tissue. Whether the blood transfusion actually stimulates the bone marrow or merely breaks a vicious circle and thus improves the nutrition of the blood-forming organs, the fact remains that it is the most powerful factor at our command for improving the quality of the blood in pernicious anemia.

When a remission is instituted as a result of blood transfusion, not only the blood picture but also the symptoms in general show improvement. The secretion of hydrochloric acid, however, does not return, nor is there any marked improvement in the spinal cord symptoms, when the latter are present.

Massive doses of blood are not required for pernicious anemia, except in the most urgent cases. Smaller amounts, that is, 150 to 400 c.c., repeated at intervals of two weeks or even less, seem to give the best results.

I have accurate records of four cases of pernicious anemia, in three of which repeated transfusions of small amounts of blood were followed by early remissions or decided improvement. In one case, that of a woman sixty-seven years old, the red blood cell count rose from 1,510,000 to 4,220,000 and the hemoglobin from 32 per cent to 57 per cent in a period of two weeks. Following two transfusions of 400 c.c. and 250 c.c., respectively, there was a decided improvement in the patient's color and general appearance and she was able to be up and around (see fig. 3).

A second patient with the addisonian anemia, a woman of sixty-seven, was admitted in an extremely critical condition with an erythrocyte count of 880,000 and a hemoglobin reading of 20 per cent. In this case, a remarkable improvement was apparently brought about by two blood

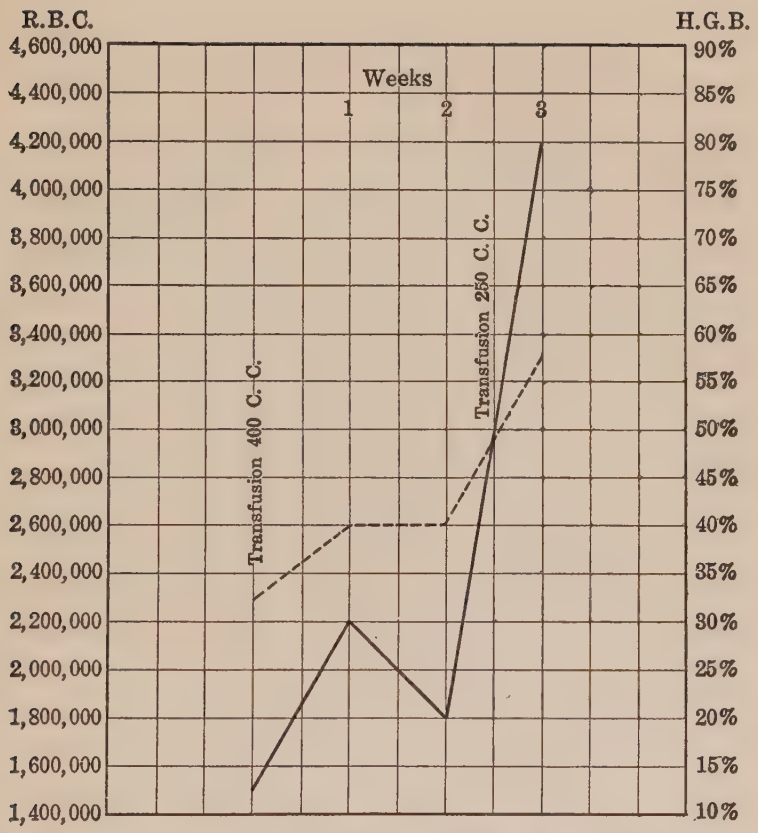

Figure 3. Effect of blood transfusions on the red blood cell count and the hemoglobin percentage in a case of pernicious anemia.

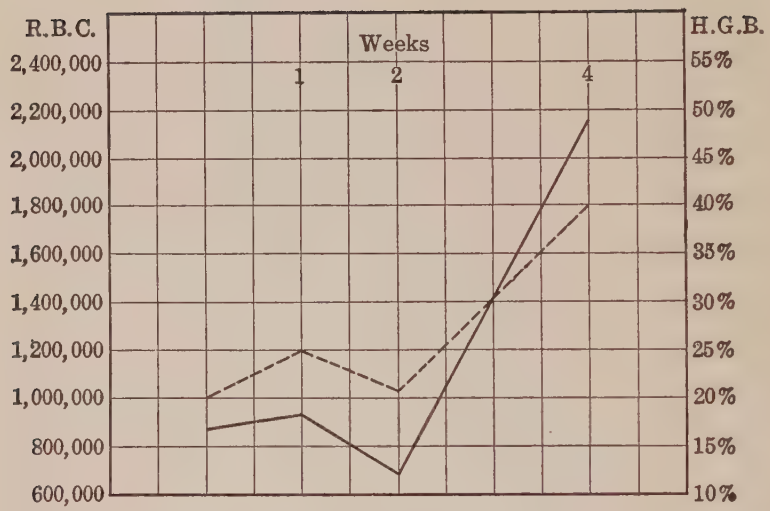

Figure 4. Effect of blood transfusions on the red blood cell count and the hemoglobin percentage in a case of pernicious anemia.

transfusions. At the end of one month, the red blood cell count had risen to 2,160,000 and the hemoglobin was 45 per cent. The patient felt greatly improved, and her color and general appearance showed a decided turn for the better (see fig. 4).

In a third case of pernicious anemia, that of a woman sixty-two years old, three blood transfusions resulted in definite improvement but the results were not so striking as in the two cases cited above.

My fourth patient, a woman twenty-eight years old, failed to show any improvement in response to repeated blood transfusions, and she died.

In all of my cases of pernicious anemia, I have noticed that, even when the hematologic picture is not improved, there is a prompt and decided abatement of the fever following blood transfusions.

Finally, although blood transfusion does not cure pernicious anemia, it may be conservatively stated that it prolongs life, ameliorates the symptoms, and, in the majority of cases, leads to a remission.

Unfavorable Reactions. Unfavorable reactions to blood transfusion in pernicious anemia seem to be more common than in other conditions. They occur, as a rule, in cases in which the same donor has been used repeatedly. Bowcock [18] has shown that such reactions may take place in spite of the most careful testing beforehand. Sometimes they are extremely severe. It would appear that this reaction results not from the occurrence of iso-agglutination but as the result of the sensitization of the recipient to foreign protein contained within the donor's blood. This topic is more fully discussed in Chapter VI (see p. 81). It is advisable to lessen the risk of this anaphylactic shock by utilizing as many different donors as possible.

The Leukemias. The results of blood transfusion in the

leukemias are unsatisfactory. Occasional cases are noted, however, in which remarkable improvement may follow. This treatment is always worth while. As a means of controlling the hemorrhagic tendency in acute lymphatic leukemia, it may be of value and may thereby prolong life for a time.

I[19] have reported a fulminating case of acute lymphatic leukemia in a woman, twenty-seven years old, with an apparent duration of only five days, in which blood transfusion yielded no benefit. I also transfused a child with a very severe acute splenomyelogenous leukemia, but there was no benefit and the patient soon died.

Secondary Anemias. In the so-called secondary anemias, blood transfusion is a valuable adjunct to treatment. The prime indication, however, is to direct attention to the causative factor. In splenic anemia and Banti's disease, blood transfusion gives temporary improvement.

(7) Subacute Systemic Bacterial Infections. The fact that blood transfusion unquestionably increases the resistance of the recipient to infection has led to the employment of this procedure in various conditions of subacute systemic bacterial sepsis. Subacute bacterial endocarditis has received the greatest attention in this respect.

Some workers have tried transfusions from immunized donors. Donors were previously immunized by vaccination with the organism obtained from the patient. The technic of this procedure is described on page 49. The most that can be said for the plan of employing immunized donors, however, is that this method is still in the experimental stage and that it may possibly be found to be of some value. Results so far have not been encouraging.

I have had twenty-one patients with subacute bacterial endocarditis and positive blood cultures for Streptococcus viridans. These patients received transfusions from non-

immunized donors. There was no apparent benefit and they all died.

(8) Acute Septic Conditions. In various septic conditions, blood transfusion has met with a certain measure of success. In cases of sinus thrombosis complicating mastoiditis, it has given excellent results. I have had ten cases of mastoiditis in which blood transfusion was requested. Seven of these patients recovered. In four cases of complicating sinus thrombosis, there were two recoveries.

Puerperal Sepsis. My experience with regard to the employment of blood transfusions in puerperal sepsis leads me to be rather optimistic. In six very severe cases in which I utilized this procedure, there were four recoveries.

Appendicitis and Empyema. In one of two cases of perforated gangrenous appendix, blood transfusion seemed to be an important factor in bringing about recovery. The other patient died. In one case of empyema a single transfusion, at a time when septic manifestations were very marked, appeared to confer definite benefit.

Bacteriemia. In frank bacteriemia, whether resulting from streptococcus or staphylococcus infection, the results are not so good as in septic conditions with a negative blood culture. Fry [20] reported six cases of bacteriemia in which transfusions from immunized donors were employed, with one recovery. Four of his patients were practically moribund. The patient who recovered had a bacteriemia with Streptococcus hemolyticus and was in an extremely critical condition. Stetson [21] reported ten recoveries in nineteen cases with a positive blood culture for Streptococcus hemolyticus, and one recovery in eight cases of Streptococcus viridans bacteriemia, and three recoveries in twelve cases of Staphylococcus aureus bacteriemia. Copher [22] transfused seven patients with streptococcus bacteriemia from non-

specifically immunized donors, but there was no improvement and all of the patients died.

I have transfused ten patients with bacteriemias (other than Streptococcus viridans infections, for which see p. 68), with three recoveries. In six cases, Streptococcus hemolyticus was the infecting organism (two recoveries); in one, Streptococcus mucosus capsulatus; in three, the staphylococcus. One of the latter patients recovered. He was a man, thirty-nine years old, with two positive blood cultures for Staphylococcus aureus. The focus of infection was an abscess of the scrotum. For six weeks this man ran a septic temperature. Blood transfusions were administered in conjunction with autogenous vaccines and supportive measures. The patient made a complete recovery.

Pneumonia. In influenzal pneumonia, Ross and Hund [23] employed blood transfusion and obtained results which would indicate that this measure may be of value. Of twenty-eight patients who received transfusions, six, or 21.4 per cent, died. On the other hand, of twenty-one patients who were not transfused, 9, or 42.8 per cent, died.

I gave blood transfusions to two moribund patients with postoperative pneumonia. Both recovered.

Typhoid Fever. In typhoid fever, Ottenberg and Libman [11] observed two recoveries in seven patients who were desperately ill. McClure and Dunn [24] reported a case in which immunized blood was given to an exsanguinated typhoid patient with an excellent result, the temperature dropping to normal and intestinal hemorrhage ceasing.

Measles. Zingher [25] has recently shown that the serum, whole blood or plasma of a convalescent from measles is capable of preventing or aborting an attack of the disease. The amount of blood required from the donor is small, that is, from 2.5 to 20 c.c. The blood is drawn from the donor into a syringe containing 1 to 2 c.c. of 5

per cent sterile citrate solution and immediately injected intramuscularly. Of 102 non-immune children injected by Zingher after exposure to measles, ninety-two children were completely protected; seven developed a mild form of the disease; only two suffered a typical attack of measles. Under ordinary circumstances, from 96 to 98 per cent of non-immune untreated children will acquire typical measles if exposed to the infection.

Ribadeau-Dumas and Brissaud [26] report the cases of two Arabs with measles who were brought to the hospital in extreme collapse. One of them recovered after the transfusion of citrated blood from a measles convalescent; but the other patient, who was not transfused, soon died.

Diphtheria. Harding [27] has obtained some experimental results on cats and rabbits which would indicate that blood transfusion may possibly prove to be of use in the toxemic stage of diphtheria.

Tuberculosis. Blood transfusion has been tried in pulmonary tuberculosis, but apparently with indifferent results. Freilich [28] and his co-workers treated six patients with pulmonary tuberculosis at weekly intervals by means of two to five transfusions, each of from 100 to 375 c.c. of blood. In no case was the clinical course of the disease altered nor was there any apparent benefit.

(9) Diabetic Coma. Blood transfusions have been recorded in the treatment of diabetic coma but the results heretofore have been mostly unfavorable. Most of these reported observations deal with treatment by blood transfusion without the concurrent administration of insulin. Raulston and Woodyatt [29] in 1914 reported a severe case of diabetic acidosis in which the transfusion of 500 c.c. of blood from a healthy donor proved decidedly detrimental to the metabolism of the patient, as evidenced by a marked rise in the output of sugar, ammonia and acetone bodies

and an increase in the glucose: nitrogen ratio. The patient died in typical dyspneic coma. Ottenberg and Libman [11] in 1915 employed blood transfusion in four cases of diabetes mellitus but failed to observe any benefit from this procedure. Three of the patients were in coma. In no case did the transfusion have more than a transient effect on the coma. Garbat [30] in 1919, after replacing 500 c.c. of blood removed from a patient in diabetic coma with citrated blood from a healthy donor, observed distinct temporary improvement and the patient came out of her coma. There was noticeable improvement after a second transfusion, but the patient soon relapsed and died.

Animal experiments have been more encouraging than the clinical trials. Carlson and Ginsberg [31] in 1915 transfused dogs rendered diabetic by pancreatectomy with blood from normal dogs. The dosage was approximately one-tenth the volume of the recipient's blood. In these experiments there was observed a definite and consistent lowering of the hyperglycemia and glycosuria, which lasted from four to eight hours. When diabetic dogs were used as donors there was no effect on the hyperglycemia.

My [32] own rather remarkable experience in a single case of juvenile diabetic coma, in which combined treatment with large doses of insulin and blood transfusions resulted in prompt recovery, would suggest the possibility that these combined measures may prove to be very valuable in the treatment of diabetic coma. The patient was a Jewish boy, ten years old, who was admitted to the hospital in deep coma, with all the clinical and laboratory evidences of diabetes mellitus and maximal acidosis. No definite improvement was noticed after large doses of insulin. A transfusion of 250 c.c. of unmodified blood in this insulin-treated patient, however, resulted in instantaneous and very marked improvement and the boy immediately came

out of coma. A second similar transfusion six hours later was again followed by striking benefit and the patient walked out of the hospital on the sixth day. One year later, he is still alive and doing well.

(10) Debilitated Conditions. In debilitated conditions in general and in wasting diseases, such as cancer for example, blood transfusion is of service as a palliative measure. It does not appear to confer any benefit in pulmonary tuberculosis (see p. 71).

(11) Miscellaneous Indications. Certain abnormal conditions for which blood transfusion has been employed that are not included in the above classification will be mentioned here. In *pellagra* Cole [33] employed blood transfusion in twenty far advanced cases of the disease. He obtained 60 per cent of recoveries as contrasted with the usual rate of 10 to 20 per cent.

Nephritis. I have employed blood transfusion in three cases of kidney disease. One patient was a girl, three years old, with acute hemorrhagic glomerular nephritis secondary to a streptococcus infection of the throat. She had been passing bright red urine for ten days. She was given a transfusion of 200 c.c. of blood and two days later there was but a slight amount of blood in the urine. Four days after the transfusion the urine was clear. The patient made a complete recovery.

In one case of chronic glomerular nephritis with a high degree of nitrogen retention, blood transfusion was of no avail and the patient soon died. In a case of nephrosis, the transfusion seemed to have no effect upon the course of the disease nor upon the symptoms.

Favorable results in the treatment of an anemia associated with the azotemia of nephritis have recently been reported by Flandin and Tzanck.[34] In one patient with hypertension and with asthma-like crises and in two with

chronic nephritis, from two to six blood transfusions were used with good results.

Eclampsia. Bell[35] has reported one case of severe eclampsia in which blood transfusion gave a very successful result.

Tropical Sprue, Acne Vulgaris. In five cases of tropical sprue, Lindeman[36] reported recoveries following blood transfusion. He also noted a striking clearing up of persistent *acne vulgaris* after blood transfusion in two patients; in one of these cases, the skin disease was associated with tuberculosis, while in the other the transfusion had been given for the treatment of illuminating gas poisoning.

Burns. Robertson[37] employed exsanguination-transfusion (see p. 131) in cases of severe burns in children and concluded that this treatment is of value. Of seven children suffering from profound toxic shock from superficial burns, showing symptoms usually considered inevitably fatal, five recovered completely.

I gave a child with an extensive surface burn a transfusion of 200 c.c. of blood, but there was no favorable effect upon the toxemia and he soon died.

Marasmus and Intestinal Intoxication of Infants. In these conditions, blood transfusion may be of great value.

Epidemic Encephalitis. According to Kerley,[38] blood transfusion has been followed by striking improvement in a few cases of epidemic encephalitis.

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CHAPTER VI

Dangers of and Untoward Results from Blood Transfusion

Five principal classes of untoward results may occur after a blood transfusion, as follows:

1. Massive agglutination and hemolysis of the recipient's or donor's cells from the use of an incompatible donor.
2. An anaphylactic reaction, presumably due to sensitization of the patient or inherited allergy to the donor's blood (most common in multiple transfusions).
3. Citrate reactions.
4. The transmission of communicable disease from the donor to the recipient.
5. Multiple embolism.

(1) Agglutination from Incompatibility. Before the discovery by Landsteiner of the various iso-agglutinins and iso-agglutinogens in blood and the division of bloods into four major groups, blood transfusion was considered to be a most hazardous procedure, to be used only as a last resort. Nevertheless the cause of this great danger was but vaguely suspected. We now know that the great majority of these disasters arose from the transfusion of blood from incompatible donors with resulting massive agglutination of the red blood cells. Nowadays, with proper preliminary blood grouping and compatibility tests, blood transfusion is a very safe procedure and untoward results from incompatibility are rare.

Cases are still reported in which unfortunate sequelae

occur after transfusion. In many instances, these results arise from the fact that the preliminary testing of donor and recipient has been inadequate. This phase of the subject is fully covered in Chapter III (see p. 25). It cannot be too strongly emphasized that, in order to avert such accidents, donor and recipient must both belong to the same blood group, that their bloods must be proved to be compatible by direct matching, and that a universal donor should be used for a recipient of a different blood group when this can be avoided.

Clinical Picture. When a blood transfusion is performed between two persons of incompatible blood groups, a typical reaction may ocur. Untoward phenomena begin to appear early, that is, after the introduction of from 50 to 100 c.c. of blood. The patient complains of tingling pains over the entire body, fulness in the head, precordial oppression, and later excruciating lumbar pain. Gradually the face becomes cyanotic, and breathing is labored. The pulse rate falls sharply, sometimes as much as twenty to thirty beats a minute. Consciousness may be lost momentarily. There may be an urticarial eruption appearing in from fifteen minutes to an hour. The most characteristic reaction is a severe chill, which is followed by a rise of temperature to 103-105° F. The urine is distinctly bloody and appropriate tests show the presence therein of a large amount of hemoglobin. This hemoglobinuria results from the hemoglobinemia which follows the hemolysis of a large number of agglutinated red blood cells. Delirium and jaundice are inconstant symptoms.

If the full amount of 500 c.c. of blood has been injected, death in a few hours is the rule. When not more than 100 c.c. has been transfused, however, the patient usually recovers. The subcutaneous administration of adrenalin and atropine may be of value in this condition.

Incompatibility of White Blood Cells. According to some *in vitro* tests reported by Doan,[1] there may be definite incompatibility between the blood plasma of certain individuals and the white blood cells of others. Owing to the fact that at least twenty-seven different combinations are possible, a blood group classification of individuals according to their white blood cell compatibility would be extremely difficult and complex. However, white blood cell incompatibility may serve to explain some hitherto obscure causes of reactions to blood transfusion. This subject requires further study.

(2) Anaphylactic Reactions. When the recipient has previously been transfused from the same donor, various anaphylactic reactions, even anaphylactic shock, may ensue. These accidents are presumably the result of acquired hypersensitiveness to the donor's serum. Such subjects are sensitized not to human serum in general but only to the serum of some particular donor. The period of greatest likelihood of anaphylactic manifestations following a second transfusion from the same donor is three to six weeks after the first transfusion. Any of the various symptoms which occur in allergic states from other causes may be present. There is usually eosinophilia. An urticarial eruption is a common manifestation of such hypersensitiveness.

A case of fatal anaphylactic shock following a first transfusion of 500 c.c. of blood by the citrate method was reported by Carrington and Lee.[2] Blood matching and group tests showed no incompatibility and there was no history which would indicate protein sensitization in either donor or recipient. The attack began with spasm of the smooth muscle of the bronchioles, bladder and intestines, as evidenced by difficult breathing, typical asthmatic râles and incontinence of urine and feces. This spasm was followed by relaxation, associated with pulmonary edema.

The temperature rose to 102° F., pulse 130 and respiration 36. After several hours, the venous blood showed hemolysis. The first symptoms did not appear until one hour after the transfusion had been completed.

Wolfe [3] reported a case in which, two hours after a blood transfusion from a compatible donor belonging to the same group, the recipient suffered a most severe reaction with acute bronchial spasm, unquestionably anaphylactic in nature. The patient recovered.

Duke and Stofer [4] reported a severe case of allergic shock, during which the patient almost died, following the transfusion of but 20 c.c. of blood from a compatible donor. The reaction in this case came on immediately after the injection of the first syringeful of blood. The patient was found by skin tests to be hypersensitive to milk, but the donor gave a negative reaction. The authors believe that the reaction was probably due to the recipient's hypersentiveness to some digestive product of milk contained in the donor's blood.

I have observed one accident, apparently of an anaphylactic nature, which occurred in a patient who had never before been transfused. A woman, thirty-five years old, with puerperal sepsis began to suffer from great difficulty in breathing only two minutes after the transfusion of but 10 c.c. of blood from a compatible donor. The face, arms and hands swelled to an enormous size and the skin took on a dusky red color. The transfusion was discontinued and adrenalin was administered subcutaneously. The patient promptly recovered. The donor and the recipient both belonged to Group II, and direct matching of the bloods both before and after the transfusion showed no incompatibility.

I have observed certain reactions in patients who were properly typed and cross-matched that are difficult to ex-

plain. After about 40 to 100 c.c. have been transfused, the patient complains of pain in the back and of "feeling queer." A few moments later, the pulse becomes irregular; it may stop. Respiration may cease, and the patient then becomes cold and cyanotic. The cyanosis begins in the face or fingers and spreads rapidly. During such a reaction, death appears imminent. However, in all of the cases that I witnessed, the patient recovered.

When such a reaction occurs, the transfusion should be discontinued at once and adrenalin administered subcutaneously. In view of the possibility of a reaction, it is always advisable to have the adrenalin in readiness for a transfusion. Reactions of this type are more likely to occur in debilitated patients.

When such a reaction occurs, it does not necessarily follow that a subsequent transfusion will be dangerous. I recall the case of a woman who had a reaction of the type described above after the transfusion of 150 c.c. of blood. However, three days later, she was transfused with 500 c.c. of blood without any untoward phenomena.

In Pernicious Anemia. Anaphylactic manifestations after blood transfusions are most apt to occur in pernicious anemia, in which condition it is necessary to give frequent transfusions, often from the same donor. These reactions may take place in spite of the most careful preliminary testing, as has been shown by Bowcock.[5] Several instances of anaphylactic shock from second transfusions of compatible blood given to patients with pernicious anemia have been reported by Böttner.[6] These accidents occurred during the three to six weeks' interval and were associated with eosinophilia.

When it is necessary to give a series of transfusions, as is often the case in pernicious anemia, it is, of course, not always possible to employ a new donor each time.

However, inasmuch as the period of the greatest likelihood of an anaphylactic reaction is three to six weeks after a blood transfusion from a given donor, it is a good plan to rotate several donors so as to greatly lessen the danger from this source.

Precautions. Anaphylactic manifestations usually appear promptly and after the transfusion of but a small amount of blood. A precaution against their onset is the slow introduction of blood during the early stage of the operation. With the appearance of symptoms, the transfusion should of course be immediately discontinued. Adrenalin administered subcutaneously is a valuable remedy for the anaphylactic state.

Cases have been reported in which the anaphylactic manifestations were delayed as long as two hours. Such accidents are unavoidable.

If a patient has demonstrated his hypersensitiveness to the blood of a given donor, it does not mean that no further transfusions should be given. A different blood donor should of course be selected and the transfusion should always be begun very slowly.

(3) Citrate Reactions. Reactions due neither to incompatibility nor to anaphylaxis are fairly common. The most noteworthy of these sequalae are the so-called citrate reactions, occurring after the transfusion of citrated blood. These reactions are not severe and serious results from this source are uncommon. The most usual manifestation is a chill followed by a rise of temperature of about 2 or 3° F. Nausea and vomiting may occur.

Similar reactions may occur after transfusions by the syringe method, but they are much more common when citrate is used as an anticoagulant. Lewisohn[7] observed chills after 8 per cent of sixty transfusions with Unger's apparatus and after 13 per cent of eighty-three transfusions

by the citrate method. He attributed the slight preponderance of chills following the citrate method to the chilling of the blood during the transfer, not to any action of the citrate itself.

Many observers, however, attribute the reaction to the citrate itself. Keynes [8] observed a case in which a slight citrate reaction occurred in a youth who had acted as a blood donor. The transfusion was carried out by a modification of the syringe method which involved the injection at intervals of a syringeful of citrate solution into the donor's circulation. In this case it is difficult to escape the conclusion that the reaction in the donor was produced by the citrate solution injected.

Pauchet [9] noted reactions in twenty-five of one hundred patients after citrate transfusions, whereas in one hundred cases in which the syringe method was employed no symptoms were noted. Lederer [10] noted reactions in 49.5 per cent of forty-seven transfusions by the citrate method, as compared with no reactions at all after forty-nine transfusions with unmodified blood. Kretzler,[11] in a series of transfusions in which the syringe method was employed thirty-seven times and the citrate method sixty-four times, likewise noted a much higher percentage of reactions in the cases in which the citrate method was used. Chills occurred in 40 per cent of these cases, and there was a rise in temperature of 3° F. or more in the same number of cases. With the syringe method, chills and pyrexia occurred in only 5 per cent of the patients. Nausea or vomiting took place after 18 per cent of the citrate transfusions as contrasted with only 2.8 per cent after transfusions of unmodified blood.

Citrate Fatalities. While fatalities due to reactions following citrate transfusion are rare, they do, nevertheless, occur. It is important to recognize the type of patient

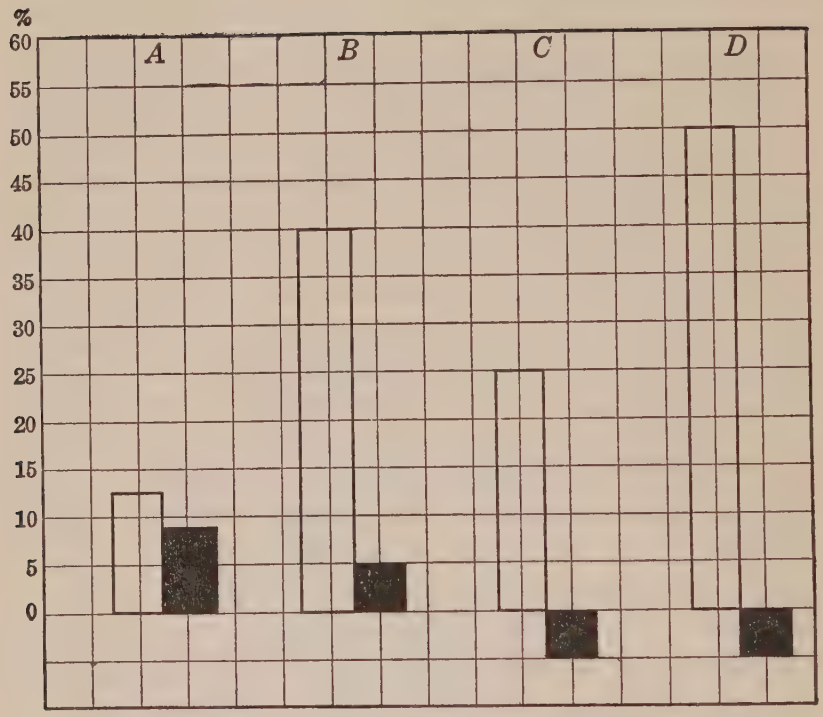

Figure 5. The relative frequency of reactions after transfusions by the citrate method and after transfusions by syringe methods, according to four different observers. White, percentage of reactions after citrate transfusions; black, percentage of reactions after syringe transfusions. A, Lewisohn; B, Kretzler; C, Pauchet; D, Lederer.

whom it is dangerous to transfuse by this method. Bernheim,[12] who has had two deaths from citrate transfusions and who has personal knowledge of four other deaths from this source, stated that the following types of patients should not be transfused by the citrate method:

1. Patients who have been so completely exsanguinated as to be in such extreme shock that the additional hazard of a citrate reaction must be avoided. Bernheim cites the case of a man, exsanguinated as the result of bleeding from a duodenal ulcer, who was transfused with 500 c.c. of citrated blood. The patient had a very severe chill, his temperature rose to 105° F., and death soon followed. All of the preliminary laboratory tests had been properly performed and there was no question of incompatibility.

2. Patients in such profound states of anemia as to be almost dead.

In my experience with the syringe method of transfusion, pyrexia due to this procedure has been uncommon, and chills rare. I believe that there is a much greater freedom from such attacks after the use of unmodified blood than after the citrate method. It does not appear, however, that, except in rare instances, the so-called citrate reactions are so alarming as to discourage one in the use of this method when a blood transfusion is indicated and the syringe methods are not available.

Anuria. Anuria following blood transfusions is a rare complication and its cause is largely unknown. Curtis[13] reported a case in which there was hematuria immediately after a transfusion by the citrate method, followed by almost complete anuria for four days. The blood urea reading rose to a figure of 100 mg. per 100 c.c. The patient recovered. It appears probable that in this case the anuria resulted from the accumulation in the kidneys of an excess of broken-down red blood cells. Bancroft[14] recently re-

ported a case in which, after the transfusion of 400 c.c. of blood by the Unger method, the patient had a severe chill and a rise of temperature. There was anuria for nine days, and the blood urea nitrogen rose to 65 mg. per 100 c.c. In this case, there was no primary hemoglobinuria and it is therefore difficult to account for the onset of anuria. Of nine cases of anuria or extreme oliguria following blood transfusion reported in the literature, seven were preceded by hemoglobinuria.

Reactions Due to Rubber Tubing. The statement has been made by Busman [15] that supposedly pure gum-rubber tubing may be responsible for some of the unfavorable reactions occurring after blood transfusion by the citrate method and after the intravenous administration of arsphenamine. According to Busman, new tubing can be rendered harmless and incapable of producing such reactions by soaking it for six hours in normal sodium hydroxide solution.

(4) Transmission of Communicable Diseases. The principal diseases which may be transmitted by blood transfusion are syphilis, malaria and measles. The operator should, on general principles, insist on the selection of a donor in perfect health; but, in addition, especial precautions should be taken to rule out the presence of any of these three diseases.

Syphilis. Syphilis is the most dangerous and the most difficult to rule out. If one follows the routine of demanding a careful history and physical examination and a Wassermann test for the purpose of excluding syphilis in the donor, this accident should be rare.

Sydenstricker, Mason and Rivers [16] reported a case in which a man was infected with syphilis as the result of transfusions *from his own son.* No Wassermann test had been made. The greatest danger lies in the use of a donor in the interval between the primary and secondary stages

of syphilis. The syphilitic infection thus transmitted is apt to be of a fulminating type.

Often in emergencies, there is no time to perform a Wassermann test. In such cases, my practice is to resort to the Kahn test.

When the donor has necessarily been selected in a hurry and there has been no time for the preliminary serologic examination, the Wassermann test should be performed after the transfusion. It has been shown that individuals who have exposed themselves to syphilis by contact with persons who are known to harbor the disease in an active form may be safeguarded by receiving two intravenous injections of arsphenamine soon after the exposure. If the Wassermann reaction of an emergency donor should prove to be positive after the transfusion has been employed, the same method of prophylaxis should be used.

Malaria. Malaria may readily be transmitted by the injection of blood from a patient who harbors the parasite. In fact, the inoculation of patients with malaria by means of the subcutaneous injection of the blood of a person infected with the disease is a measure now employed by some workers in the treatment of general paresis.[17]

Van Dijk [18] reported a case in which the recipient was infected with malaria following the injection of serum from a convalescent patient. This observation shows that malaria may thus be transmitted even though the donor is not having active chills at the time.

I have observed a similar case. The donor, who was the patient's father, had had malaria many years previously but had been free from symptoms for a long time. The recipient, a female child, developed typical malaria and the parasites were found in her blood.

If it should be discovered immediately after transfusion that the donor is harboring malarial parasites, the outbreak

of the disease in the recipient may be prevented by immediate treatment with quinine.

Measles. Measles may be transmitted by means of blood transfusion, but this accident is fortunately rare because of the fact that the recognition of the disease is usually obvious. Bauguess[19] has reported two cases in which blood transfusion from a mother who was subsequently found to have measles resulted in the transmission of the disease to the child. A similar case has been reported by Harrell.[20] Such accidents are apt to occur in the early catarrhal stage of measles, when the disease may easily escape recognition. They emphasize the importance of refusing to use a donor who does not appear to be in perfect health.

If, after a transfusion, one should discover that the donor has measles, it is not too late to prevent the disease. It has been shown that the injection of convalescent serum, plasma or whole blood is an efficient means of measles prophylaxis after exposure to the disease (see p. 70). For the details of this treatment and the dosage to be employed, the reader is referred to Zingher's[21] paper.

Allergy. Ramirez[22] reported a case of bronchial asthma with allergy to horse dander which was transmitted by means of blood transfusion. The first attack appeared two weeks after the injection of 600 c.c. of blood. Both donor and recipient were subsequently found by skin tests to be extremely sensitive to horse dander.

(5) Multiple Embolism. Although it is a rare accident, multiple embolism undoubtedly does occur and it may lead to sudden death. The danger of this complication is greatest when transfusions are employed in the treatment of subacute bacterial endocarditis or puerperal conditions. The onset of this complication comes like a bolt out of a clear sky. During or immediately after the transfusion,

the patient, who has previously been doing well, abruptly stops breathing and dies.

I have experienced one such accident in a girl, twelve years old, with subacute bacterial endocarditis and a growth of Streptococcus viridans from her blood. The child appeared in good condition at the beginning of the transfusion, but suddenly stopped breathing and collapsed. All attempts at resuscitation were in vain.

In patients whose condition predisposes them to embolism, the transfusion should be performed as slowly as possible and should be instantaneously discontinued on the appearance of any untoward symptoms. This accident is so rare, however, that it may be safely said that the possible benefit which may accrue from blood transfusion to patients suffering with subacute bacterial endocarditis or puerperal infection or hemorrhages far outweighs the dangers.

Air Embolism. In the past, emphasis has been laid on the dangers of air-embolism resulting from the introduction of air-bubbles during intravenous procedures. These dangers appear to be more theoretical than real. Robertson and Brown [23] have shown that after the introduction of as much as 10 c.c. of air into the femoral vein of a dog, only momentary cyanosis is produced thereby, from which the animal soon recovers without bad after-effects. Of course, the introduction of air-bubbles should be avoided, when possible, on general principles.

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CHAPTER VII

Methods of Performing Blood Transfusion

Introduction. A great many methods of performing blood transfusion have been described and many forms of apparatus have been devised. Many of these methods embody no new principles but merely modify procedures already in use. In this chapter, no attempt will be made to survey completely the field of technical measures. Only those methods of transfusion which are in common use, which possess distinct merit or which, though now obsolete, represent an epochal advance in the history of blood transfusion will be described.

Certain technical details are common to all methods of performing blood transfusion. In describing the different procedures, therefore, it will not be necessary to repeat this detailed description in each instance but merely to point out the features which are peculiar to the individual operations. In Chapter VIII (see p. 106) I shall give a complete description of my own method of performing a blood transfusion. For a more minute exposition of those steps in the performance of a blood transfusion which are common to most of the methods, the reader is advised to supplement the description of the various procedures given in the present chapter by reference to Chapter VIII.

Crile's[1] Direct Cannula Method. This method, though now obsolete, merits description because of the fact that it was the first practical procedure for performing blood transfusions on man. The success which attended blood

transfusion by Crile's method gave this form of therapeutics its greatest impetus and inspired the general interest in this subject which ultimately led to the invention of the simple instruments of today. For this direct method of transfusion a small cannula was used, through which the recipient's vein was drawn and cuffed back over the cannula. The donor's artery was then pulled over the vein so as to establish a continuous intima coat.

Technic. The radial artery of the donor is chosen because of its accessibility and the ease with which it can be connected with one of the veins on the inner surface of the recipient's elbow. Twenty minutes before the transfusion, a hypodermic injection of morphine is given to both donor and recipient. The donor and recipient, with their heads pointing in opposite directions, are placed on separate tables of such construction that the head can be instantly lowered. If symptoms of shock should appear, in either donor or recipient, the patient is immediately placed in the Trendelenburg position.

Under infiltration anesthesia with 0.1 per cent cocaine (0.5 per cent novocaine would be better) about 3 cm. of the radial artery is exposed and the small branches are tied with very fine silk. A "Crile" clamp is then applied to the proximal end of the artery and the distal end is ligated. The artery is severed between these two points. The adventitia is pulled over the free end as far as possible and closely snipped off. The field is then covered with a moist saline sponge.

The donor being ready for the transfusion, attention is next turned to the recipient. An accessible vein is selected, usually one of those at the bend of the elbow, and the area is infiltrated with cocaine or novocaine solution. Three or four centimeters of this vein are then exposed in the same

manner as the donor's artery. The distal portion of the vein is ligated and a "Crile" clamp is applied to the proximal end. The vein is then divided and the adventitia is drawn out as far as possible and closely snipped off.

The vessels are now ready for attachment to the cannula. The cannula (see fig. 6) comes in various sizes. The donor's artery and the recipient's vein should be examined, and a cannula should be selected whose bore is a little larger than the actual tissue thickness of the larger of these vessels. The vein is then pushed through the tube and its free end is turned back like a cuff and snugly tied in the second groove (fig. 6). In the meantime, an assistant steadies and manipulates the handle of the cannula by means of a forceps. The donor's artery is now pulled over the vein and tied snugly with a small linen ligature in the first groove (fig. 6). The anastomosis is now complete.

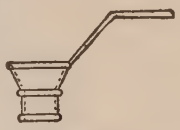

Figure 6. * Crile's cannula (twice actual size)

The transfusion takes place when the clamps are removed from the artery and the vein. First the clamp is removed from the vein, then the clamp on the artery is gradually released. The passage of blood from the donor to the recipient will be detected when the latter's vein is seen to dilate and a pulse is palpated therein. A larger stream of blood may be maintained by the application of warm saline solution and by protecting the vessels from the air. These measures serve to relax the artery wall.

When the transfusion has been completed, the vessels are ligated and the cannula removed. Skin sutures are then inserted and a dressing placed over the incisions.

An unfavorable feature of this operation is the fact that there is no means of accurately measuring the amount of blood transfused. One must make a crude approximation

* Reproduced by courtesy J. B. Lippincott Company.

from the fullness of the pulse in the recipient's vein, the duration of the transfusion, and the clinical condition of donor and recipient.

Method of Kimpton and Brown.[2] This is an indirect method of performing blood transfusions, coagulation being avoided by the reception of the donor's blood into a receptacle which is smoothly coated with paraffin. This procedure has largely been superseded by the citrate method. The chief objection lies in the fact that, unless the tube and its connection are smoothly coated with a uniform layer of paraffin, the blood is apt to clot.

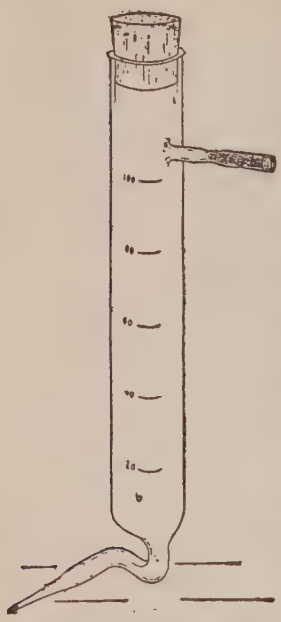

Figure 7.* The Kimpton-Brown tube, of 100 c.c. capacity. A similar tube of 700 c.c. capacity will be found more convenient. (Kimpton and Brown, J. A. M. A.)

The Kimpton-Brown Tube. The Kimpton-Brown tube (see fig. 7) is a glass cylinder closed at the upper end by a cork stopper and possessing a perpendicular side-tube a little below the cork and an S-shaped cannula leading from the bottom of the cylinder. The Kimpton-Brown tubes come in various sizes, but the most convenient one has a capacity of 700 c.c. and is marked at increments of 50 c.c. up to 500 c.c. The cylinder originally described by Kimpton and Brown has a capacity of only 100 c.c. A rubber double-bulb bellows is attached to the perpendicular side-tube.

Paraffinization of Tube. The most difficult part of the transfusion is the preliminary coating of the tube with paraffin. A small piece of pure, clean paraffin with a melt-

* Reproduced by the courtesy of the American Medical Association.

ing point of 50° C. is placed in the cylinder and the cork is inserted. The tube is then wrapped in a towel, placed on its side in an autoclave and sterilized. The sterile tube is then removed from the towel and warmed over the flame of a Bunsen burner or an alcohol lamp. During the heating, it is carefully revolved, so as to allow the melted paraffin to cover all parts of the inner surface of the cylinder, the cork and the side tube. The excess is then allowed to run out of the cannula, the tip being held against a sterile gauze sponge. In order to avoid excessive crystallization of the paraffin, rapid cooling of the cylinder is necessary. This can be effected by contact with the operator's hand. In order to prevent contamination of the contained blood from the air when the rubber bellows is used, a small piece of sterile absorbent cotton is loosely inserted into the side-tube as far as the constriction. The cylinder is now ready for use. Great skill and dexterity are required to paraffinize these tubes properly. If there is the smallest defect in the paraffin coating, coagulation will take place within the tube.

Procedure. After infiltration of the area with 0.5 per cent novocaine solution, one of the donor's veins at the bend of the elbow is exposed (see p. 118). An oblique incision is made into the vein so as to produce a flap which may be raised by means of a pair of artery forceps. The point of the cannula is then inserted into the vein so as to point toward the hand. The cannula is then pushed in until the widest part engages the whole circumference of the vein. Pressure is then made upon the upper arm by constricting it with a rubber tube. The blood usually flows rapidly into the Kimpton-Brown tube. When the desired amount of blood has been obtained, the constriction is released and the Kimpton-Brown tube is withdrawn from the donor's vein. A ligature, previously placed around the vein peripherad to

the incision, is immediately ligated by an assistant; as an alternative, pressure may be maintained by means of a sterile swab.

The operator immediately carries the tube filled with blood over to the recipient. From the moment of withdrawal the end of the cannula should be closed by the right index finger in order to prevent the escape of blood. An assistant exposes one of the recipient's veins in the same manner as was done for the donor. In the case of the recipient, however, the cannula should be directed toward the head. A similar flap is made in the wall of the vein, and the cannula is pushed into the vein until its

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Figure 8. The Kimpton-Brown tube, filled with blood, held so as to keep the blood from running out while inserting into the vein of the recipient. (Kimpton and Brown, J. A. M. A.)

widest part engages its circumference, as was done in the case of the donor. In order to force the blood from the tube into the recipient's circulation, a rubber double-bulb bellows is attached to the side-tube and operated. One must be careful to remove the positive pressure before the tube is completely emptied of blood; otherwise air will be introduced into the circulation. When it is nearly empty, the Kimpton-Brown tube is withdrawn and the vein is tied. The skin of donor and recipient is then sutured and dressings are applied.

Lewisohn's [3, 4] Citrate Method. This simple and safe method of blood transfusion is still extensively used because it can be employed by the untrained physician. The technic

of this method, as commonly employed, was perfected by Lewisohn, but credit for priority is due to Hustin and Agote (see p. 9).

The principle of this method is the addition of sodium citrate in a concentration of 0.2 per cent to the blood removed from the donor for the purpose of preventing coagulation and the immediate reinjection of this citrated blood into the recipient. A full discussion of the anticoagulative

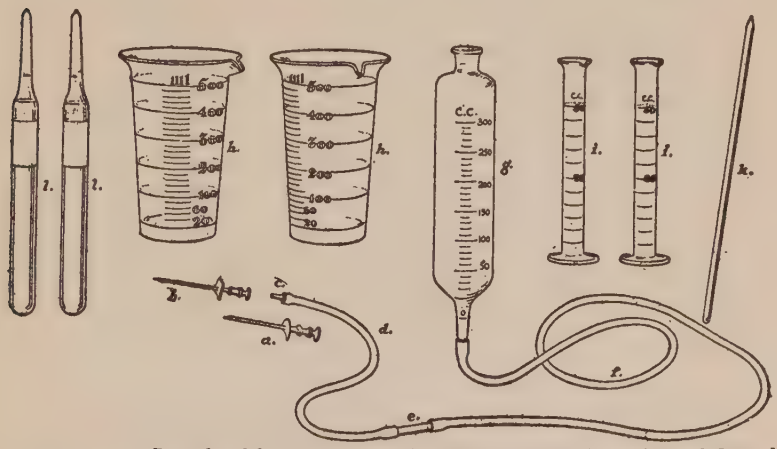

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Figure 9. Complete outfit for transfusion of blood by Lewisohn's citrate method. a and b, cannulæ; g, salvarsan flask with rubber tubing; d, f, glass taper connect (e) and adapter (c); i, small glass jars; h, two large glass jars; k, glass rod; l, two glass ampoules containing 50 c.c. of a sterilized 2.5% solution of sodium citrate. (Lewisohn, Boston M. & S. J.)

properties of sodium citrate and of the alleged harmfulness of this salt will be found in Chapter II (see p. 16).

Technic. The complete apparatus required for this method is shown in figure 9.

After the preparation of the donor's arm (see p. 111), the tourniquet is applied above the elbow and a large needle (10 to 14 gauge) is inserted directly into one of the veins at the bend of the elbow. It is better to point the needle in the direction of the hand. The blood is allowed to flow rapidly into a large glass jar containing 25 c.c. of a 2.5 per

cent sterilized solution of chemically pure sodium citrate. After about 250 c.c. of blood have been obtained, 25 c.c. more of the citrate solution are added. The blood and anticoagulant are mixed by gentle agitation and stirred by means of a sterile glass rod. Rough handling must be avoided, as it may damage the corpuscular elements. When the desired amount of blood has been obtained (usually about 500 c.c.), the needle is withdrawn from the donor.

For the introduction of the blood into the recipient, the apparatus used for the administration of salvarsan by the gravity method may conveniently be employed. The citrated blood is transferred from its glass container into the salvarsan-flask by filtering through gauze. Lewisohn believes that if the blood and citrate solution are mixed rapidly, no clots—not even minute ones—will form. In that event, straining of the blood through gauze before the injection of the citrated blood into the recipient would be entirely unnecessary. The citrated blood should be injected as soon as possible after its withdrawal from the donor and, in the interval, should be kept warm by placing the jar in a basin of warm water. Lewisohn has suggested that it would probably be an easy matter to prevent chilling of the blood during transfer by the use of a thermos bottle of special construction. Such a bottle would have to be made so as to enable us to determine exactly how much blood has been taken from the donor. While they would be expensive and fragile, and not accessible to the average practitioner, such bottles would, nevertheless, probably be a valuable addition to the armamentarium of those physicians who use the citrate method as a routine.

In puncturing the vein of the recipient, a smaller needle is used, as there is no longer the danger of clotting with its consequent need for a rapid flow. In the case of the recipient, the needle should point toward the head. When

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Figure 10. Taking the blood from the donor for transfusion by the citrate method. (Lewisohn, Boston M. & S. J.)

the veins are small and collapsed, as not infrequently happens in patients requiring transfusion of blood, it may be necessary to incise the skin under novocaine anesthesia and to expose the vein. When the latter has been entered, about 50 c.c. of saline are run in and then the stop-cock is released and the citrated blood is allowed to flow by gravity.

The need of maintaining constant asepsis renders the citrate method more cumbersome than the syringe procedures now in common use. The addition of an anticoagulant certainly constitutes a theoretical objection, although it has not been proved that the citrate is in any way injurious. This method is particularly applicable to military surgery and industrial injuries. In rural districts and other places where facilities are not at hand, the citrate method is often the only one that can be employed.

Citration of Blood within the Donor's Needle. Instruments have been devised which operate on the principle of citrating the blood within the donor's needle. It is claimed that the number and severity of reactions may thus be reduced 50 per cent. For the details of these methods, the reader is referred to the papers by Hartman [5] and by Cowles and Antz.[6]

Transfusion with Preserved Red Blood Cells. This method was devised during the World War as an emergency procedure and proved very valuable in the rush periods during attacks, when there was no time for the usual methods. Robertson [7] has shown that blood may be bottled as long as twenty-six days prior to transfusion. There is experimental evidence to show that erythrocytes may be artificially preserved as long as thirty days and that, when transfused, they will then functionate (see p. 23). The red blood cells are preserved in isotonic solutions of sodium citrate and dextrose. Only persons belonging to Group I (Janský), i.e. universal donors, are selected, as, in emergen-

cies, there is no time for preliminary testing of the recipients. It would be possible, however, to have each soldier marked so as to identify his blood group, previously determined. During the intervals, the blood is stored in an ice-box. Robertson's results with this method of transfusion were encouraging. The advantage of having a large quantity of blood at hand in anticipation of the casualties of an active encounter is obvious. For the details of this method, the reader is referred to Robertson's [7] article.

Lindeman's [8, 9] Method (Syringe-Cannula System). This is a cumbersome and difficult method, which requires a skillful team of workers. In expert hands, the Lindeman

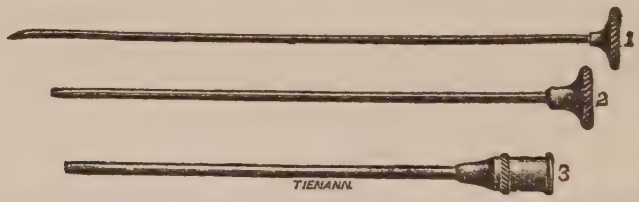

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Figure 11. Lindeman's set of three cannulæ. 1, innermost cannula (hollow needle); 2, middle cannula; 3, outer cannula. (Lindeman, J. A. M. A.)

method has yielded good results; but the procedure requires too much dexterity and coöperative skill to appeal to the average worker.

Six Record syringes and two sets of cannulas, three to each set, are required. A constant circulation of syringes is kept up, the latter being filled with blood from the donor, emptied into the recipient and washed in rapid succession.

Apparatus. The entire equipment consists of six 20 c.c. Record syringes, two tourniquets and two sets of cannulas, one for the donor and one for the recipient. Each of these sets of cannulas (see figs. 11 and 12) consists of three cannulas, telescoping one within the other. The innermost cannula is a No. 30 gauge; at one end it is ground to a fine point with a short bevel. It fits snugly into the second can-

nula. The outermost cannula is a No. 14 gauge and it is capped with a receiver to fit any Record syringe.

Technic. The donor and the recipient lie in parallel positions and a small table is placed between them. On this table there are three basins containing sterile physiologic sodium chloride solution at approximately room temperature. These basins are for the washing of the syringes. The nurse at this table washes each syringe, after its contained blood has been injected into the recipient, by rinsing it successively in each of the three basins. The syringes are cleaned as rapidly as they are used.

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Figure 12. Lindeman's set of three cannulæ, telescoping one within the other. A, distal end of cannula 2; B, distal end of cannula 3. (Lindeman, J. A. M. A.)

One operator manages the syringe of the donor; the other, that of the recipient. The skin at the bend of the elbow is sterilized (see p. 113), and the tourniquet is then applied to distend the vein. Acting simultaneously, the operators for the donor and recipient, respectively, insert the cannulas into the vein of the donor and that of the patient. It is better to allow the donor's cannula to point toward the hand and the recipient's toward the head. When the needle has entered the vein, a drop of blood trickles from the distal end of the innermost cannula. After the first joint, A (fig. 12), has entered the vein, the innermost cannula is withdrawn about one-half inch. This prevents the vessel wall from being injured by the needle after further entrance of the cannula into the vein. With the thumb on the screw-cap of the middle cannula, the entire cannula is forced further along until the joint

B enters the vein. The middle cannula is then withdrawn a distance of one-half inch. The outermost cannula alone is now in contact with the vessel wall. This cannula is pushed gently into the vein to the desired distance, which is usually from three-quarters to one inch, and the tourniquet is then removed. An obturator is inserted until the syringe is ready.

When both donor's and recipient's veins have been properly entered, as described above, the obturator is removed from the donor's needle and an empty syringe is attached and filled with blood. This syringe is then rapidly passed to the recipient's operator and the donor's operator promptly replaces it with a fresh syringe. The recipient's operator removes the obturator from the cannula, attaches the syringe and promptly evacuates its contents into the vein. The emptied syringe is then passed to the nurse for rinsing, being immediately replaced by the second syringe from the donor. Thus the syringes follow each other in rapid succession, until the desired quantity of blood has been transfused. As the syringes contain 20 c.c. each, the amount of blood transfused is easily calculated by simply counting the number of syringefuls of blood injected. Occasionally a little salt solution is squirted around the cannula in order to keep the field clean, but none is injected into the vein.

Unger's [10, 11] Method of Syringe Transfusion. The instrument devised by Unger (see fig. 13) utilizes the principle of a syringe and a two-way stop-cock. This method is very simple and reliable and is easily learned. Because of its simplicity and sound mechanical construction, Unger's instrument has earned deserved popularity. It is open to the theoretical objection, however, that the presence of a chamber, wherein the stop-cock rotates, allows of a possibility of a reflux of blood from recipient to donor.

Unger's Apparatus. The essential feature of Unger's

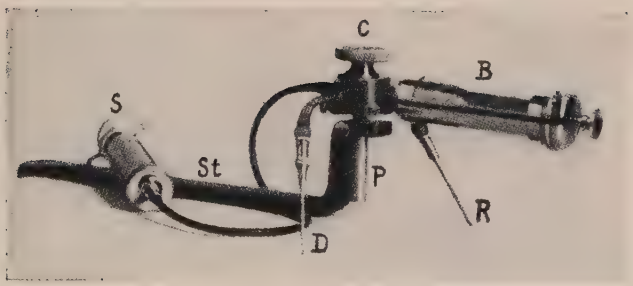

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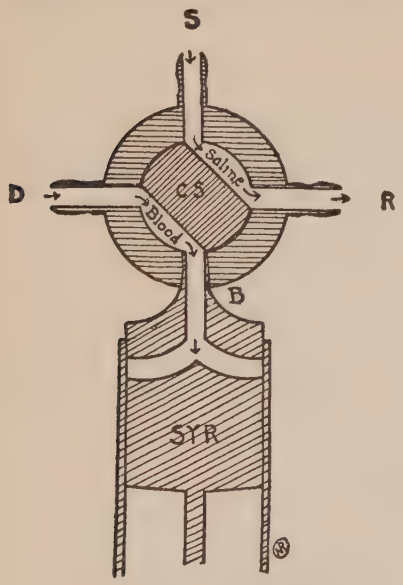
Figure 13. Unger's instrument for syringe transfusion: C, stop-cock; B, blood syringe connected to blood outlet; S, saline syringe connected to saline outlet; D, donor's cannula connected to donor's outlet; R, recipient's cannula connected to recipient's outlet; St, stand; P, pedestal by which the stop-cock is raised or rotated. (Unger, J. A. M. A.)

instrument consists of a stop-cock which alternately connects a syringe for blood to the donor and at the same time one for saline to the recipient. When the stop-cock is turned, the syringe for blood is connected to the recipient,



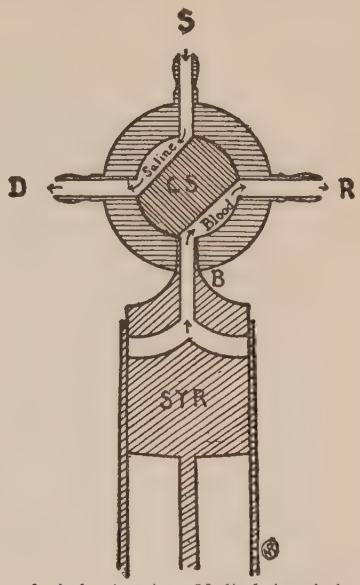


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Figure 14. Diagram of Unger's transfusion apparatus in donor's position: D, donor's outlet; B, blood outlet; Syr., blood syringe. Blood passes from donor's vein through D, out at B into Syr. S, saline outlet; R, recipient's outlet. Saline is forced from saline syringe through S, out at R, into recipient's vein. Channel between D and B, donor blood circuit; that between S and R, recipient saline circuit. CS, central stopper (rotates through an arc of 45 degrees). (Unger, J. A. M. A.)

Figure 15. Diagram of Unger's transfusion apparatus in recipient's position: Syr., blood syringe; B, blood outlet; R, recipient's outlet. Blood is forced out of Syr. through B, out at R, into recipient's vein. S, saline outlet; D, donor's outlet. Saline is forced from saline syringe through S, out at D into donor's vein. Channel between B and R, recipient blood circuit; that between S and D, donor saline circuit. CS, central stopper. (Unger, J. A. M. A.)

while that for the saline is connected to the donor. Figure 14 shows the connections of the outlets in the donor's position, that is when the blood syringe is connected to the donor's vein, while figure 15 shows how the outlets communicate when the instrument is in the recipient's position.

Technic. The donor and the recipient lie in parallel positions with their arms on the board between them (see p. 112). The donor's needle points toward the hand, the recipient's, toward the head. After the veins of the donor and recipient have been entered by the needles (see p. 115), the tubes leading from the instrument are connected. The stop-cock is placed in the donor's position (see fig. 14), a 20 c.c. Record syringe is inserted, and blood is aspirated. When the syringe is filled, the assistant turns the stop-cock and the operator injects the blood into the recipient. The stop-cock is then turned back to the donor's position, and this procedure is continued until the desired amount of blood has been transfused. The amount of blood transfused may be easily calculated at any time, as each syringeful injected represents 20 c.c. While the syringe is being filled with and emptied of blood, a stream of ether is sprayed upon it.

In the meantime, the assistant slowly injects saline, thus flushing alternately the circuit of the recipient and that of the donor. It is not necessary to change the syringe for blood after each injection, but only when it begins to work with difficulty. While the syringe is being removed and replaced by a clean one, the stop-cock is turned to the intermediate position, thus preventing a loss of blood.

[1] Crile, G.: The technic of direct transfusion of blood. Ann. Surg., 46:329, 1907.

[2] Kimpton, A. R. and Brown, J. H.: A new and simple method of transfusion. J. A. M. A., 61:117, 1913.

[3] Lewisohn, R.: A new and greatly simplified method of blood transfusion. Med. Rec., 87:141, 1915.

[4] Lewisohn, R.: The citrate method of blood transfusion after ten years: A retrospect. Boston M. & S. J., 190:733, 1924.

[5] Hartman, F. W.: Transfusion reactions and citration within the needle. J. A. M. A., 78:15, 1922.

[6] Cowles, G. E. and Antz, H. W.: New apparatus for blood transfusion with the citrate method. Surg., Gynec. & Obstet., 37:841, 1923.

[7] Robertson, O. H.: Transfusion with preserved red blood cells. Brit. M. J., 1:691, 1918.

[8] Lindeman, E.: Simple syringe transfusion with special cannulas: A new method applicable to infants and adults: preliminary report. Am. J. Dis. Child., 6:28, 1913.

[9] Lindeman, E.: Blood transfusions without a chill by a syringe-cannula system: Two hundred and fourteen consecutive cases. J. A. M. A., 72:1661, 1919.

[10] Unger, L. J.: A new method of syringe transfusion. J. A. M. A., 64:582, 1915.

[11] Unger, L. J.: Recent simplification of the syringe method of transfusion. J. A. M. A., 65:1029, 1915.

CHAPTER VIII

The Author's Method of Performing Blood Transfusion

Introduction. Most operators who are called upon frequently to perform blood transfusions have adopted some one of the various vein-to-vein syringe methods now in vogue. There is no question but that, once learned, these syringe procedures are superior to the use of modified blood, in that the injection of citrated blood gives rise to a definitely higher percentage of reactions (see pp. 82-85). The citrate method, however, is still extensively used and is preferred by some workers.

In devising his instrument, the author had in mind the two following ideals:

(1) To reduce the difficulties of instrumental manipulation to a minimum.

(2) To obviate, by the elimination of any chamber wherein the blood of donor and recipient may mix, the possibility of a reflux of blood from the recipient to the donor.

The recipient is *always* a sick man, and his blood is very frequently capable of transmitting disease. The donor has nothing to gain by his donation, save possibly a fee. Common justice, therefore, demands that he be accorded the fullest measure of protection.

The Author's Instrument. The instrument devised by the author[1] (see fig. 16) consists essentially of two disks, rotating one upon the other through an angle of 90°. The proximal disk is perforated to form a channel for communication with a Record syringe attached to it; this open-

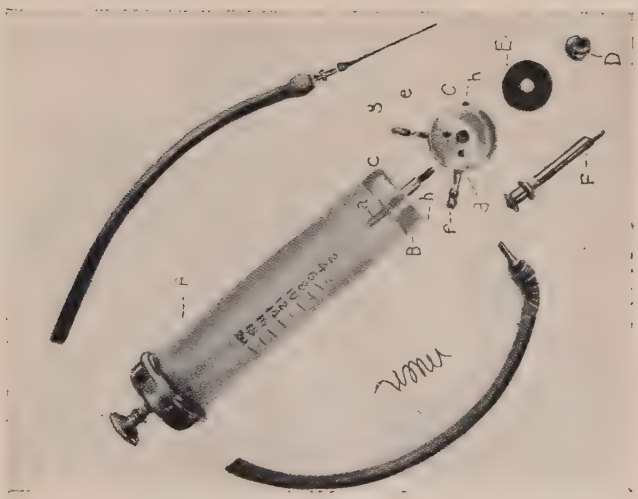

Figure 17. The Feinblatt transfusion apparatus, showing the component parts: A, twenty c.c. record syringe. B, proximal disc; a, metal tube; b, shaft threaded at the extremity; c, marking showing whether communication is with inlet or outlet. C, distal disc; d and e, openings communicating with inlet and outlet tubes respectively, f and g, each of which alternately comes into apposition with the single opening in the proximal disc, as the discs are rotated; h, stop regulator with two projecting arms. D, nut. E, steel spring washer. F, needle for use in infants.

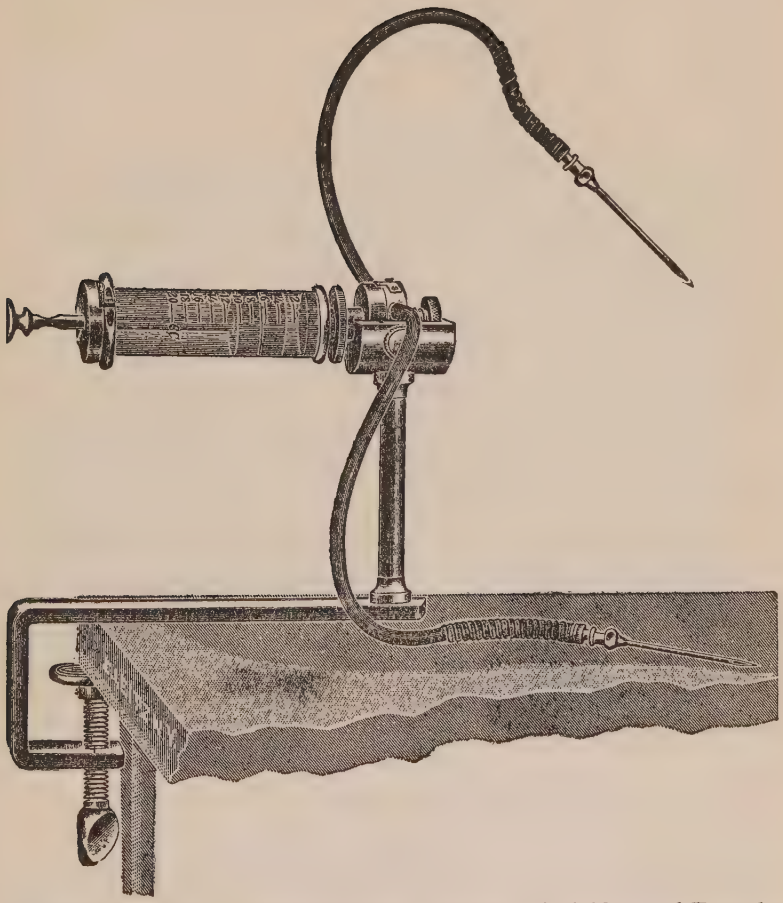

Figure 16. The Feinblatt transfusion apparatus. (Feinblatt and Eggerth, Clinical Laboratory Medicine, published by Wm. Wood & Co.)

ing alternately becomes continuous with either of two similar openings in the peripheral disk, for the inlet and outlet respectively.

The component parts of the machine are illustrated in figure 17. *A* is an ordinary 20 c.c. Record syringe. Its tip fits into the proximal disk of the instrument. The disks are made of brass, heavily nickeled, and measure one inch in diameter by five-sixteenths of an inch in thickness. The proximal disk (*B*) is continued into a metal tube (*a*) for the reception of the tip of the syringe. On its distal surface, the proximal disk is continued into a shaft (*b*), which is inserted into the distal disk, thus allowing rotation of the disks one upon the other. The terminal portion of the shaft *b*, which, when inserted, projects beyond the distal disk, is threaded for the reception of the nut (*D*). Midway between the center and the circumference, the distal surface of the proximal disk is perforated by an opening, which communicates with the syringe. There is a small pin on the circumferential surface of the proximal disk, which, by limiting further movement as it strikes against the projecting arms of the stop-regulator (*h*), provides for the correct angle of rotation of 90°. A mark on the circumferential surface shows whether the syringe is connected with the inlet or the outlet, that is, with the donor or the recipient.

The distal disk of the instrument (*C*) has a large opening in the center for the reception of the shaft of the other disk. Midway between the center and the circumference, its proximal surface discloses two openings (*d* and *e*), similar to the single foramen in the other disk. These openings are separated by an angle of 90° and they represent channels which become continuous through the disk with those of the outlet and inlet tubes (*f* and *g*) respectively. The range of motion is limited to 90° by the stop-

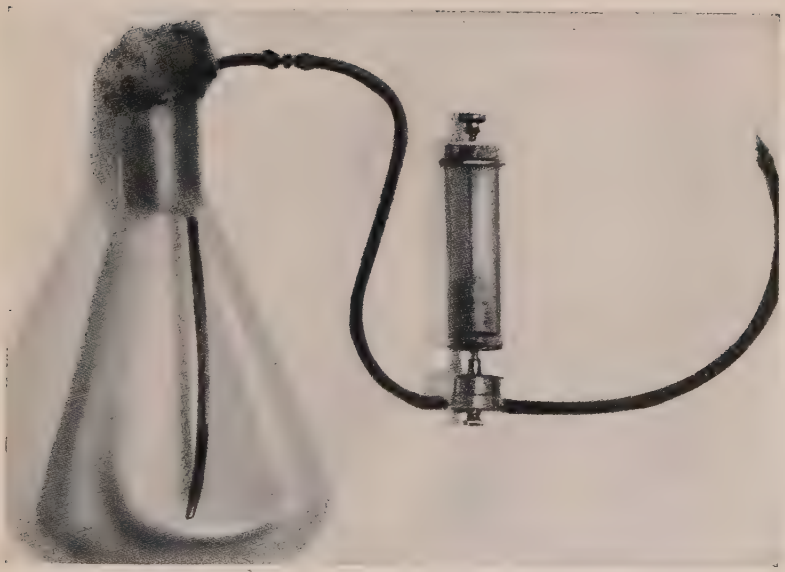

Figure 18. The Feinblatt transfusion apparatus adapted to the performance of hypodermoclysis.

regulator (*h*), which is screwed on to the circumferential surface of the distal disk. A steel spring washer (*E*) is interposed between the nut and the distal disk.

To both the inlet and the outlet there is attached a piece of rubber tubing with an adapter. In order to keep the end of the tube bent in any desired position, there is a wrapping of wire at this junction with the adapter.

The machine, with the inlet and outlet projecting upward, may be held in the slotted holder (see fig. 16), which is clamped on to the board or the table. Personally, I prefer not to use the holder.

I have used this instrument successfully in the performance of more than 350 blood transfusions. For ease of manipulation and sureness of result, I believe it to be superior to any other instrument with which I am acquainted.

This instrument, it has been found, may be utilized not only for blood transfusions but also for various other procedures, including intravenous infusion, hypodermoclysis (see fig. 18), phlebotomy and the withdrawal of fluids from the body cavities.[2]

Armamentarium. I make it a rule to have the following equipment prepared for a blood transfusion:

1. The Feinblatt transfusion apparatus. This may be sterilized by boiling or by placing in 50 per cent. alcohol for twenty minutes. The rubber tubing should be detached for sterilization and afterwards attached to the inlet and outlet respectively.

2. Six needles of the Record or Luer type. For adults, a No. 15 or 16 gauge is suitable; for older children, a No. 17 or 18 gauge (see p. 120). The gauge of the needle selected in an individual case depends on the size of the subject's veins. The needles should have a rounded, bevelled edge; they should not taper to a point. The

long-pointed needle is too apt to traverse the entire width of the vein and perforate the opposite wall. I prefer needles without the flange, as the weight of the latter is apt to pull the needle out of the vein. The wrapping of wire around the end of the tubing near the adapter amply serves to hold the needle in place. The needles should be equipped with well fitting stylets so that they may be kept perfectly clean.

3. A narrow pine board or a flat tray, on which to work and on which the arms of the donor and recipient are placed. This board should measure about two feet in length by ten inches in width and one-half inch in thickness.

4. Several 20 c.c. Record syringes. Some workers prefer smaller syringes (2 c.c., 5 c.c. or 10 c.c.). I see no advantage in the use of the smaller syringes. Usually it is not necessary to change the syringe, but it is wise to have others on hand in case this should become necessary.

5. A little sterile albolene, for the purpose of lubricating the plunger of the Record syringe.

6. An ethyl chloride spray. This is to be used when it is desirable to freeze the barrel of the Record syringe. This freezing is seldom necessary; it should be employed to prevent clotting of the contained blood in case there should be any delay in the operation. I prefer ethyl chloride to ether because of the more convenient form for spraying in which it is put up. When blood clots in the syringe, causing it to stick, an ethyl chloride spray will readily loosen the clot so as to allow the syringe to be cleansed.

7. Three sterile sheets: one for the patient, one for the donor, and one for the board.

8. Four sterile towels.

9. Ample supply of sterile gauze squares.

10. Basin containing 500 c.c. of cold sterile normal saline solution.

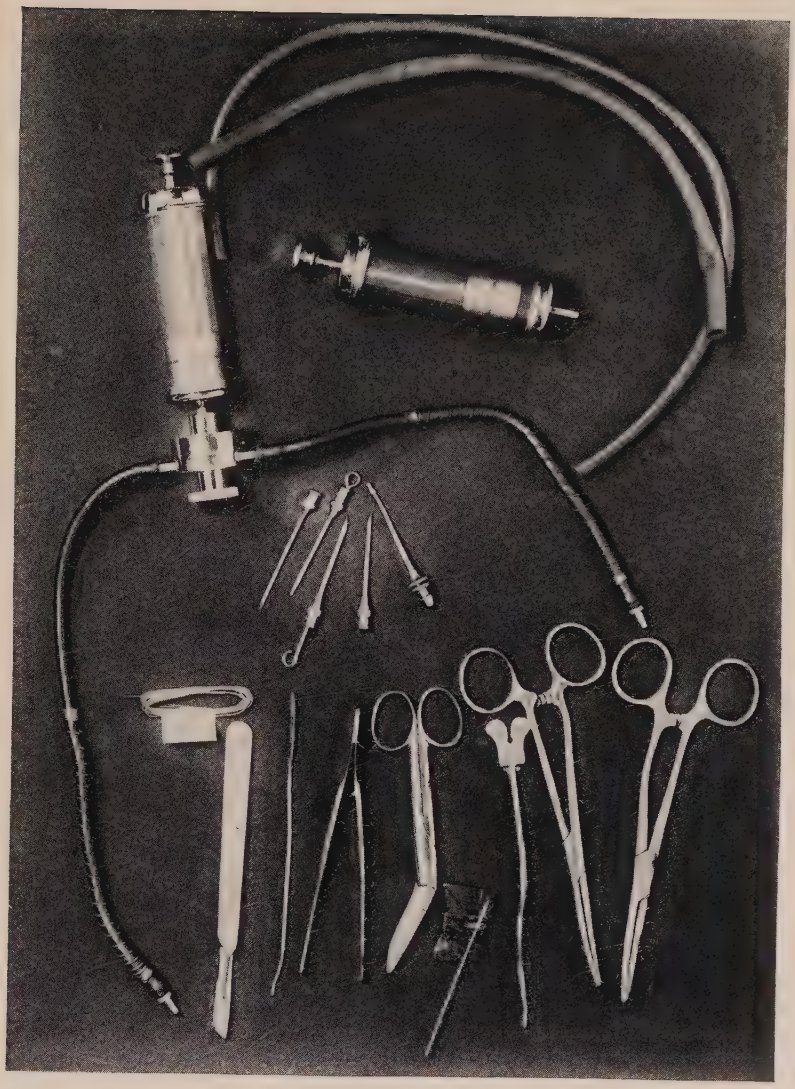

Figure 19. Armamentarium for performance of blood transfusion by author's method.

11. Alcohol, 50 per cent.
12. Tincture of iodine, 3 per cent.
13. Two strips of rubber tubing and two artery clamps, as tourniquets.
14. Sterile gowns and gloves for the operator, his assistant and the nurse.

For Exposing Vein. The following additional equipment is also prepared, in case it should be necessary to cut down on the recipient's vein:

1. Novocain solution (0.5%) with hypodermic syringe and extra fine needles.
2. Scalpel with Parker blade.
3. Small pair of scissors.
4. Thumb forceps.
5. Grooved director.
6. An eyed probe.
7. Catgut.
8. Black silk.
9. Skin needles.

In hospital practice, the preparation and sterilization of the equipment for transfusion may be left to a competent operating room staff. When it is necessary to perform the transfusion in a private home, it is convenient to have the entire armamentarium sterilized beforehand and done up in a package.

Preparation for Operation. After the armamentarium is ready, the further preparation for operation consists of the following steps:

1. Decision as to the amount of blood to be transfused.
2. Bringing the donor and the recipient together.
3. Preparation of the operative field.

(1) *Amount of Blood to be Transfused.* The factors which guide one in the determination of the amount of

blood to be transfused are the age of the patient (whether adult or child), his weight and his clinical condition. Halbertsma [3, 4] has found that in children the additional 15 c.c. of blood for each kilogram of body weight will increase the red cell count by about one million (see p. 120). Such an amount also serves conveniently as an average dose. Such a calculation, however, cannot very well be used in the case of adults. The usual practice is to give about 500 c.c. to an adult of average size. The maximal amount of blood transfused, save under the most exceptional circumstances, is 750 c.c. If more than this amount is transferred, it is advisable to employ more than one donor.

The degree of exsanguination or anemia and other clinical factors with reference to the patient's illness are of course of paramount importance. One should not hesitate to deviate from the average dosage when the clinical condition of the patient indicates such a course.

(2) *Bringing Donor and Recipient Together.* The donor is always brought to the patient. If the patient is in good condition, he should be brought to the operating room on a wheel carriage. If it is deemed inadvisable to move the patient, the donor should be brought up to the ward and allowed to lie on a wheel carriage alongside the recipient. The bed may be raised to the same height as the carriage by means of a chair placed under it.

Assuming that the transfusion is to be performed in the operating room, donor and recipient are placed on tables in parallel position, lying head to head. The arm of the patient which shows the more accessible veins is selected. If the recipient's right arm is the better, he lies on the left-hand table; whereas if his left arm is better, he lies on the right-hand table. The board is then set between the tables, and recipient and donor are instructed to place their arms on this board so that they lie in parallel positions

Figure 20. Sterile package containing armamentarium for blood transfusion, for use in private home.

with a few inches of space between the elbows. The recipient places his arm in a position which he finds comfortable, and the donor is made to adapt his position accordingly.

(3) *Preparing the Operative Field.* The operator stands at the head end of the tables, just in front of the board. His assistant stands opposite him, that is, between the tables. The nurse, with her tray, takes her position to the outside of the donor's table, regardless of whether the donor is on the right or the left table. The entire operative personnel wear sterile gowns and gloves.

The tourniquets are then placed loosely around the arms of donor and recipient. I prefer to use a plain piece of rubber tubing, about three-eighths of an inch thick, which is held in place and tightened, when desired, by means of an artery clamp. The artery clamp should always be placed so that its handle points toward the subject's head, so that the instrument will be out of the way during the operation. The tourniquet may be instantly tightened by simply pulling on the ends of the tubing and fastening the artery clamp. When it is desired to remove the constriction, the artery clamp is unfastened.

The hand of the donor and that of the recipient are covered with sterile towels as follows: The subject makes a fist, over which the towel is thrown in the manner of a bag. The free ends, after encircling the wrist, are tied with a single knot. The three sterile sheets are now placed, one over the donor, one over the recipient, and one over the board.

The operative field of patient and of donor is prepared as follows: The area at the bend of the elbow and all of the surrounding field that is to remain exposed is washed first with 50 per cent alcohol, then with 3 per cent tincture of iodine solution, and again with alcohol. Sterile towels are

then placed and pinned so as to leave only this sterilized operative field exposed.

The transfusion instrument with its rubber tubing connected is placed on the board, being clamped or not according to individual preference. I prefer to use the instrument unattached. The Record syringe is filled with the sterile normal saline solution and connected with the apparatus. The instrument should first be tried with saline solution, in order to test its freedom from obstruction and its cleanliness. The instrument and its connections should then be flushed with saline, and the syringe should contain at least 10 c.c. of this solution.

Selection of Vein for Puncture. The veins of the elbow and forearm which are accessible for the purpose of blood transfusion are shown in figure 22. The veins most commonly used are the median basilic and the median cephalic. The former is usually the larger and the easier to enter; in some cases, however, the median cephalic is the more suitable. In some subjects, these veins may be unusually small; in others, especially obese persons, they may be buried in a layer of subcutaneous fat. Often, although the vein is not visible, it can be felt as a distinct cord under the palpating finger when constriction is applied. In other cases, the vein can be neither seen nor felt but can, nevertheless, be reached by making a deep puncture in its known anatomic location.

As a rule, when neither the median basilic nor the median cephalic vein can be entered, it is better not to pursue this course any further but to cut down upon either of these veins (see p. 118).

Performance of the Transfusion. The tourniquet on the arm of the recipient is tightened so as to make the veins stand out. The patient is handled first, as the difficulties of entering the vein are likely to be much greater in his

Figure 21. Method of covering hand of donor and of recipient with sterile towel.

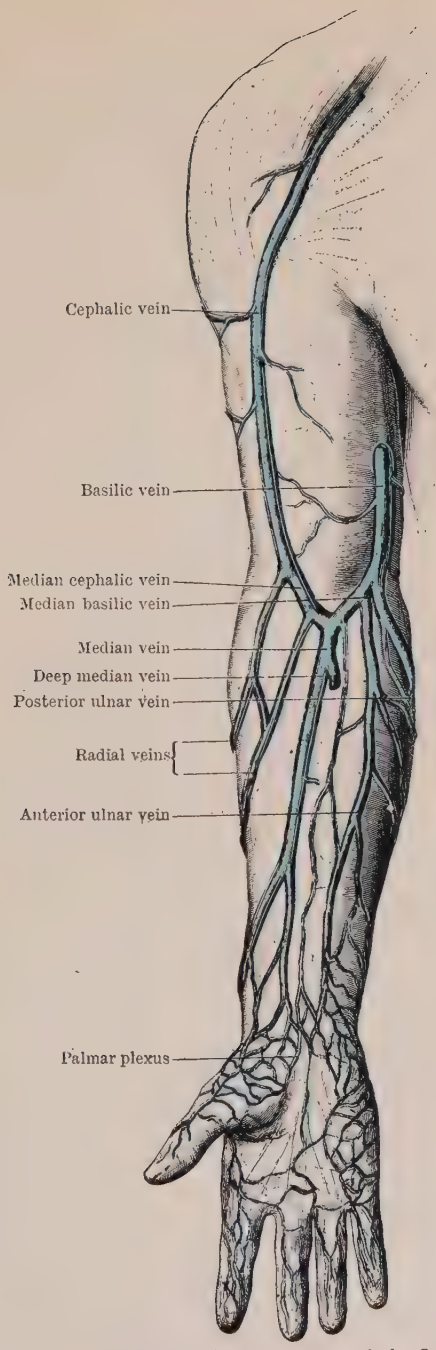

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Figure 22. Superficial veins of the flexor aspect of the upper extremity. (Cunningham, Text-Book of Anatomy, published by Wm. Wood & Co.)

case. In the selection of a donor, one would of course prefer a subject with large superficial veins. Next the radial pulse is felt, as the constriction must never be so tight as to occlude the arterial circulation. If the pulse does not come through, the tourniquet must be loosened.

Puncturing the Vein. The operator places his thumb on the vein about an inch below the contemplated site of puncture. With his thumb he steadies the vein during the puncture and keeps it from moving around in the soft subcutaneous tissue and thus eluding the needle. In the case of the recipient, the point of the needle is directed toward the shoulder. My practice is to hold the needle with the bevel pointing upward at an angle of about 15° with the skin surface. First the skin directly over the vein is punctured by means of a *short,* quick jab; the needle is then pushed into the vein with a slow motion. The moment blood begins to flow, the tourniquet should be released. The cannula is then gently pushed along for a short distance in the axis of the vein, so that it will not slip out.

The adapter appertaining to the outlet tube of the instrument is instantly inserted into the shoulder of the needle, and, the instrument having been turned to the recipient's position, the saline solution contained within the Record syringe is slowly injected. This prevents blood coagulation and insures the patency of the recipient's system of channels.

There are different ways of puncturing a vein for intravenous procedures. The method described above is the one which I personally have found best.

A procedure described by Eggerth,[5] for the purpose of obtaining blood for culture, may be used as an alternative method of puncturing a vein for the performance of blood transfusion. The thumb and forefinger of the left hand are placed on either side of the vein, so as to stretch the

skin, and the needle is inserted directly over the vein. The needle is held at an angle of 45° with the patient's forearm, with its bevel *down.*

The recipient's vein having been entered, attention is next turned to the donor, while the assistant takes charge of the instrument connected with the recipient. The donor's tourniquet is tightened, so as to distend the veins but not to occlude the pulse, and his vein is punctured in the same manner as was done for the recipient. In this case, however, the point of the needle is directed toward the wrist, not toward the shoulder as in the case of the patient. The needle is manipulated so as to obtain a free flow of blood and the adapter of the inlet tube is then inserted into the shoulder of the needle. The instrument is now connected with both donor and recipient and everything is ready for the actual transfer of blood.

Operation of the Instrument. In manipulating the instrument so as to change from the donor's to the recipient's position, and *vice versa,* hold the distal disk between the thumb and first two fingers of the left hand and rotate the syringe with the right hand. The proximal disk is attached to the syringe and is therefore rotated at the same time with it.

Turn the syringe so as to connect it with the donor. The venous pressure in the latter's vein will quickly cause the syringe to fill up with blood. The filling of the syringe may be accelerated by gently withdrawing the piston. The instrument is then switched to the recipient's position by simply turning the Record syringe with one hand, while the other hand steadies the distal disk of the instrument. In this manner, the two disks are made to rotate upon each other through an angle of 90°, and the recipient's position is obtained.

The first syringeful of blood is injected *very slowly* and

Figure 23. Arm of donor and of recipient prepared for blood transfusion. The donor's needle points toward the hand; the recipient's, toward the shoulder.

the patient is closely watched for the appearance of any untoward phenomena. Anaphylactic reactions, if they occur—and they cannot be predicted—may usually be expected to take place within a short time, often two minutes or less (see p. 79).

After the first syringeful has been injected slowly and without mishap, the transfusion proceeds more rapidly. The attached syringe is immediately turned so as to place the instrument in the donor's position again, and the syringe is refilled. All that is necessary to transfer the communication with the syringe from the donor to the recipient, and *vice versa,* is to turn the syringe with one hand while the other hand holds the distal disk, thus rotating the two disks one upon the other.

The amount of blood injected is known at all times, inasmuch as the syringe contains 20 c.c. The number of cubic centimeters administered may be rapidly calculated by multiplying the number of syringefuls injected by 20.

The amount of blood to be transfused having previously been calculated, it is only necessary to divide this figure by 20 in order to find out how many syringefuls should be injected.

Five hundred cubic centimeters or more may be injected very rapidly. After the injection of the first syringeful, which proceeds very slowly, I make it a practice to complete the operation rapidly. It has been said that too rapid a transfusion of blood may embarrass the recipient's circulation and that a dry cough is a signal of this distress. According to my own experience, this must be a very uncommon occurrence, and I therefore favor a rapid transfusion.

As a rule, one Record syringe will be sufficient for a transfusion. Should the syringe show any tendency to gum, however, the instrument should be placed in the intermediate position (with the circumferential marking half-way

between the two projecting arms of the stop-regulator) and the Record syringe replaced with a clean one. The gummed syringe may be rinsed with saline and returned.

It is seldom necessary to use the ethyl chloride spray. When, for any reason, some delay takes place in the midst of the transfusion, ethyl chloride should be sprayed on the barrel of the syringe for the purpose of retarding coagulation.

After the transfusion has been completed, the transfusion apparatus should be washed free of blood in cold saline solution, then in alcohol and ether. The needles are rinsed with cold water or saline, then with alcohol and ether, and a small drop of oil is placed on the stylet, which is inserted.

Exposing the Vein. When the recipient's veins are so small or so deeply buried that they cannot be entered by skin puncture, it becomes necessary to expose one of the veins at the bend of the elbow. Either the median basilic or the median cephalic may be thus utilized, but I prefer the former.

The skin on the inner surface of the elbow is rubbed with 50 per cent alcohol, then 3 per cent tincture of iodine solution, and again with the alcohol. The tourniquet is then applied and tightened as for the ordinary puncture through the skin (see p. 115).

An area of skin about one inch square, including the median basilic vein at the bend of the elbow is anesthetized by means of infiltration with 0.5 per cent novocain, using a fine hypodermic needle. An incision about an inch in length is then made *parallel to the known direction of the median basilic vein.* I am opposed to the common practice of making the incision at right angles to the course of the vein, as I believe that everything possible should be done to conserve the vein for future transfusions. It is usually a simple matter to expose the vein by careful

Figure 24. Author's method of holding transfusion apparatus and syringe, without the use of the holder.

dissection; if necessary, however, one should not hesitate to elongate the incision.

When the vein has been exposed, an eyed probe threaded with catgut is slipped beneath it. The catgut is allowed to encircle the vein, its free ends being held by a clamp. *It is not tied.* This provisional ligature is placed only as a precautionary measure, as the vein should never be tied unless this procedure becomes necessary.

With the vein exposed, it is a simple matter to insert the needle into it. The tourniquet is then instantly released. In some cases it may be advisable to tie the needle in. When the needle is removed, bleeding is easily controlled by pressure.

It may be found that in previous attempts to puncture the vein through the skin the needle has traversed the vein so as to produce a second puncture higher up. In such cases it is wise to insert a blunt cannula and tie it in.

After the transfusion has been completed and the needle withdrawn from the vein, the latter is examined for oozing. If this is absent, or so slight as to be controllable by pressure, the provisional catgut ligature is removed and the skin closed by means of one or more black silk sutures. If there is any considerable amount of bleeding, the vein should be ligated below the site of the puncture.

If no assistant is available, it is a simple matter for one man to perform this operation alone.

[1] Feinblatt, H. M.: A simple apparatus for blood transfusions. Med. J. & Rec., 122:143, 1925.

[2] Feinblatt, H. M.: An instrument utilizable for various operations: Blood transfusion, hypodermoclysis, intravenous infusion, phlebotomy and withdrawal of fluids from body cavities. Am. J. M. Sc., 169:870, 1925.

[3] Halbertsma, T.: Over de doseering van het bloed bij bloedtransfusies. Nederl. Tijdschr. Geneesk., 66:1272, 1922.

[4] Halbertsma, T.: The amount of blood to be transfused in anemia of children (blood dosage). Am. J. Dis. Child., 24:269, 1922.

[5] Feinblatt, H. M. and Eggerth, A. H.: Clinical Laboratory Medicine, published by Wm. Wood & Co., 1925, p. 304.

CHAPTER IX

Blood Transfusion in Children

Introduction. In discussing the subject of blood transfusion in children and infants, four important phases wherein the practice differs from that employed in adults must be considered:

(1) The indications (see Chapter V, p. 52).

(2) Special problems relating to compatibility in children, for a discussion of which see page 31.

(3) The dosage of blood to be transfused.

(4) The differences in the technical procedures.

In the present chapter, reference will be made to the dosage to be administered to children, to the methods of gaining access to the veins, and to the routes which must be substituted (superior longitudinal sinus, external jugular vein and peritoneum) when the ordinary veins cannot be entered.

Dosage for Children. That there exists in simple anemia, in the case of children, a direct relation between the body weight, the amount of blood transfused and the resulting increase in the red blood cell count has been shown by the studies of Halbertsma.[1, 2] This investigator showed that it may be expected that, following the injection of 15 c.c. of blood per kilogram of body weight, there will be a rise in the hematologic count of approximately one million cells. In general, this figure may be used to calculate the average amount given to a child for a single transfusion. For

example, a child weighing 22 lbs. would receive a transfusion of 150 c.c. of blood. This result is obtained as follows:

$$\frac{22 \text{ (weight in lb.)}}{2.2 \text{ (changing to kg.)}} \times 15 \begin{pmatrix}\text{no. of c.c. of blood allowed} \\ \text{for each kg. of body weight}\end{pmatrix} = 150$$

Transfusion in Children. In children over two years of age, the procedure is very much the same as in adults, with the exception of the dosage as noted above. In larger children, a No. 17 or 18 gauge needle may be used; in small children, however, a very fine needle, that is a No. 19, 20 or even 21 gauge, should be selected.

Often when no other vein is accessible, the internal saphenous vein of a child at the ankle will furnish a convenient site for puncture. The upper end of this vein, in the thigh, also may be used, as suggested by Alabaster.[3]

In children under two years of age it is usually necessary to cut down on the vein; in infants under one year, practically always. In infants, or in children with very small vessels, the vein should be exposed in the manner described on page 118 and the needle directly inserted. The incision, in the case of a baby, should be as small as will possibly allow access to the vein. I believe this method to be much preferable to puncture of the superior longitudinal sinus, as it is devoid of danger. In infants under six months, the veins are very superficial, lying immediately beneath the skin. It is necessary to be extremely careful in dissecting out the vein, otherwise one may go right through it.

In performing autopsies on babies and dissecting their peripheral veins, it has always appeared to me that the latter are of sufficient size to be used for blood transfusion. I believe that the peripheral veins can and should be used for the great majority of blood transfusions on babies.

Transfusion in Newborn Infants by Way of External Jugular Vein. The external jugular vein, as has been shown

by Falls,[4] can be readily exposed in young children and even in newborn infants through a small incision in the neck. The infant is placed on a special holding board, to which his ankles and wrists are tied by means of bandages. An assistant then rotates the head to one side, so as to expose the opposite external jugular vein. After the skin over the vein has been painted with iodine followed by alcohol, the region selected for incision is infiltrated with a small amount of 0.5 per cent novocain or 1 per cent apothesin. The vein can be readily seen and is especially prominent when the baby cries. An incision about 1 inch long is made through the skin and platysma myoides muscle parallel with the course of the vein. The latter is exposed, grasped with fine artery forceps and stripped of its perivascular connective tissue. With the assistance of a grooved director, a double ligature is placed beneath the vein. The loop in the catgut is then cut, leaving the two ligatures beneath the vein. The ends are caught by mosquito forceps. The ligatures are then pulled, one upward and the other downward, so as to raise the portion of the vein to be opened clear of the wound. This maneuver stops all circulation in it. By means of fine iridectomy scissors, an incision is made half way through the diameter of the vein. A No. 19 gauge Luer needle, the point of which has been ground down with an emery wheel, is then placed in the vein, and the injection of salt solution is begun. The vein of the donor is then entered and the transfusion completed as described on page 116. After the needle is withdrawn, the ligatures which were placed early in the operation are tied above and below. The wound is closed by means of one catgut suture in the platysma muscle and a single black silk suture in the skin.

In case it should be desired to transfuse the baby by the

citrate instead of the syringe method, the semicircular incision through the wall of the infant's vein is delayed until after the blood has been obtained from the donor. The exposed vein, with the ligatures placed, is dropped back into the wound and a pad soaked in salt solution is placed over it. The blood is obtained from the donor as described on page 97, and, after the needle has been placed in the recipient's vein, first salt solution, then citrated blood, is run in.

Puncture of Superior Longitudinal Sinus. In infants under eighteen months of age, the anterior fontanelle is patent, and it is not difficult to pierce the superior longitudinal sinus, which lies directly beneath the skin. In newborn infants with collapsed veins, this sinus furnishes a means whereby blood may be directly introduced into the vascular system.

Skillfully performed, transfusion via the anterior fontanelle is generally considered to be a safe procedure. However, considering the rigid wall of the sinus and the fact that the entire operation is performed blindly, it would appear that there must necessarily be a certain amount of risk of epidural or subdural hemorrhage. Falls[4] has observed one case at necropsy, after blood transfusion by the anterior fontanelle given by a man who claimed to have had considerable experience in this method, in which a large hematoma was found under the dura. The needle had evidently penetrated the side wall of the sinus during the transfusion. I prefer, wherever possible, to cut down on the most prominent vein, either one of the veins at the bend of the elbow or the internal saphenous vein.

Technic. The operation is painless. The scalp over the anterior fontanelle and the surrounding region is shaved, rubbed with 50 per cent alcohol, then with weak iodine solu-

tion, and again with the alcohol. The child's head is steadied by the nurse. A very fine needle should be used, and it should be rounded to a short bevel.

Standing in front of the baby, the operator holds the needle at an angle of about 50° with the plane of the fontanelle and then inserts it in the midline, halfway between the center and the posterior angle of the fontanelle. The point of the needle is directed forward. A little force is required to push the needle through the tough pericranium. Once the sinus has been entered, blood begins to flow. As the sinus lies immediately beneath the pericranium, the point of the needle should not be more than one-eighth of an inch below the surface of the skin. If blood does not begin to flow at once, it may mean that the needle has been inserted too far; in that event, by slightly withdrawing the needle, the flow of blood may be started.

After the blood has begun to flow, giving evidence that the sinus has been entered, the transfusion may be continued by the syringe method (see p. 116) or by the citrate method (see p. 96). One should carefully watch the fontanelle for the appearance of swelling, which would be a sign that the blood is being injected outside of the sinus. Immediately such swelling appears, the transfusion must be discontinued.

Precautions. Anatomic anomalies of the superior longitudinal sinus are not rare. Sometimes this channel is exceedingly small; occasionally it divides into two throughout a part of its course. These variations, when present, render the procedure difficult and somewhat hazardous.

One must be absolutely certain that the needle is *at all times* actually in the sinus. The result of injecting a considerable quantity of blood outside of the sinus would, of course, be disastrous. The child's head must be kept ab-

solutely steady throughout the procedure. Any pronounced movement of the head might result in the withdrawal of the needle from the sinus or a perforation of the wall.

It is rarely necessary to utilize the superior longitudinal sinus for the performance of blood transfusion. I dislike the blind work which this procedure entails and the unhappy consequences which might follow a slip in the technic. In my experience, it is very seldom that one is unable to enter a baby's vein by properly cutting down on it.

Intraperitoneal Transfusion. Blood, when injected into the peritoneal cavity, does not coagulate rapidly and, to a large extent, is reabsorbed. In Chapter II (see p. 20) experiments have been cited to show that blood left in the peritoneal cavity is speedily taken into the circulation. This avenue, therefore, furnishes an additional means of performing blood transfusion under conditions in which the veins are so small and collapsed as to be entirely inaccessible. The investigations of Sansby [5] and Siperstein [6] and those of Ruh and McClelland [7] have thus far yielded very encouraging clinical results from the employment of intraperitoneal transfusion in infants.

Technic. Unmodified blood may be transfused by the peritoneal route by means of the author's blood transfusion apparatus, or the citrate method may be used.

When the syringe method is used, the technic differs in no wise from the description in Chapter VIII (see p. 106) except with reference to the location of the recipient's needle or cannula. The latter, which should preferably be a No. 20 gauge needle, is inserted midway between the symphysis pubis and the umbilicus, a little to one side of the median line. One should first be careful that the bladder is empty. When giving a transfusion intraperitoneally, I usually administer from 40 to 80 c.c. of blood.

For intraperitoneal transfusion by the citrate method, the abdominal puncture is made as described above, and the transfusion is given by the gravity method (see p. 96).

[1] Halbertsma, T.: Over de Doseering van het bloed bij bloedtransfusies. Nederl. Tidschr. Geneesk., 66:1272, 1922.
[2] Halbertsma, T.: The amount of blood to be transfused in anemia of children (blood dosage). Am. J. Dis. Child., 24: 269, 1922.
[3] Alabaster, G. H.: Simple method of blood transfusion in infancy. Brit. M. J., 1:263, 1925.
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CHAPTER X

Auto-Transfusion and Exsanguination-Transfusion

Auto-Transfusion. By auto-transfusion is meant the introduction into the circulation of the patient's own blood, which has been lost from the blood vessels as the result of internal hemorrhage. The first auto-transfusion, according to published reports, was performed by Thies.[1] This gynecologist cited three cases of ruptured ectopic gestation in which the free blood was bailed out of the abdominal cavity, mixed with salt solution and injected into the veins of the patient. All of these patients recovered. Schweitzer[2] performed twenty-one auto-transfusions in cases of ruptured tubal pregnancy; from his experiences he concluded that this procedure is life-saving. Schweitzer believes that the safety of auto-transfusion depends on three factors: namely, freedom from infection, absence of blood clots and the preservation of the intact condition of the red blood cells.

Goder[3] compiled fifty-two cases of tubal abortion, rupture of the spleen and of the liver, and gunshot wounds of the spleen and lung in which the extravasated blood was reinfused. These patients were all in a critical condition; nevertheless, all but one recovered.

In the closed abdominal cavity, free blood shows much less tendency to clot and undergo decomposition than when exposed to air. At the same time, disintegration undoubtedly goes on, but at a much slower rate. Only blood derived from a recent hemorrhage is suitable for auto-transfusion. The older the blood, the less the value of the red

blood cells as oxygen-carriers and the greater the danger of unfavorable reactions.

In America, White[4] successfully performed auto-transfusion in a case of rupture of the liver in which the abdomen was found to be filled with blood. In Canada, Appleby[5] employed auto-transfusion in nine cases of ruptured extrauterine pregnancy, all of the patients recovering.

In a case in which splenectomy was performed and the operation was very bloody, Burch[6] successfully performed auto-transfusion and returned a little over 800 c.c. of citrated and strained blood into a vein at the bend of the elbow. Although the patient was exsanguinated and in severe shock at the time of the operation, he nevertheless made a good recovery. In cases of this type, that is, in which the blood is reinjected immediately after the hemorrhage and there is no question of stagnation, the safety of and benefit from auto-transfusion would appear to be most promising.

Experimentally, Rossi[7] induced abdominal hemorrhage in fifteen dogs and reinfused their blood. Two of the animals developed symptoms of severe toxic reaction and one of them died. In the other dogs, the condition was favorably influenced by the auto-transfusion.

Rossi believes that the microscopic examination of the extravasated blood is an important preliminary measure to auto-transfusion. From the microscopic appearance of the erythrocytes, as regards shape, size and color, he believes that one can reach a decision as to their functional vitality and consequently as to the safety of auto-transfusion.

Indications for Auto-Transfusion. Auto-transfusion is, at best, an emergency procedure, to be performed only when, because of lack of time or some other contingency, a compatible donor cannot be obtained for a transfusion by the usual methods. The principal conditions in which

a large amount of unclotted blood is apt to be found in the peritoneal cavity are ruptured ectopic gestation, rupture of the spleen or liver, and gunshot wounds of the abdomen. In these conditions, the patient is usually exsanguinated, and it is of advantage for the surgeon to realize that this blood may be returned to the circulation with a *relative* degree of safety and with probable benefit.

As noted below, however, unfavorable reactions and even fatalities have been recorded following auto-transfusion. Whenever possible, it is always better to perform compatibility tests and select a suitable donor. Only when a healthy compatible donor cannot be obtained should one begin to think of auto-transfusion. The occasions on which this emergency arises must be uncommon.

Untoward Results. If the blood contained within the peritoneal cavity shows any tendency to clot, it is unfit for use, as there will probably be present concomitant decomposition changes in the red blood corpuscles. Stagnant blood should not, of course, be injected, because of the danger of introducing protein degradation products; the red cells contained within such blood are probably useless as oxygen-carriers. There must be no question as to the presence of infection in the abdominal cavity; otherwise, the possibility of causing a bacteriemia by auto-transfusion constitutes a grave danger.

Following auto-transfusions, reactions have been reported. They are more common than after transfusions from donors. The most common untoward symptoms are marked cyanosis, dyspnea, pains in the thorax, convulsions and chills. The reactions are attributed to decomposition changes taking place in the blood during its stay in the peritoneal cavity.

A fatality due to profound hemoglobinemia following auto-transfusion was reported by Grossman.[8] He attrib-

uted death to the intoxication resulting from the injection of blood which had been biologically modified during its stay within the peritoneal cavity. Another death from auto-transfusion was reported by Schäfer.[9]

Technic. The performance of auto-transfusion, according to the technic described by Appleby,[5] is simple. While the surgeon is opening the abdomen, an assistant inserts a needle into a vein at the bend of the elbow (see p. 115) and starts a flow of sterile normal saline solution. The apparatus used for the administration of salvarsan by the gravity method is suitable for this saline injection. If the peritoneal cavity is found to contain a large quantity of blood, this material is examined with a view to reaching a decision as to the advisability of the performance of auto-transfusion. If the blood is entirely free from clots and is not too old, it is suitable for reinjection; but if there is any doubt in this respect, it is better not to use such blood. Of course, if there is any question as to the presence of infection within the abdominal cavity, auto-transfusion would be dangerous.

If it has been decided to perform auto-transfusion, the blood is gently ladled (or sucked by means of an aspirator) out of the abdominal cavity and filtered through about eight thicknesses of gauze moistened with normal salt solution into a beaker containing about 200 c.c. of normal saline. When all of the blood has been collected from the peritoneal cavity, it is poured into the jar from which the salt solution is already entering the circulation and is allowed to flow in by gravity. Large amounts, even up to a liter or more, may be injected. There does not appear to be any real danger from circulatory embarrassment as the result of the introduction of a large quantity of fluid (see pp. 48-49).

White[4] recommends the removal of the blood from the

abdominal cavity by means of a Balfour aspirator and the addition of sodium citrate as an anticoagulant. The nozzle of the aspirator is introduced into the peritoneal cavity and the blood is collected into a receptacle which contains 50 c.c. of 2.5 per cent sodium citrate. If more than a pint of blood is aspirated, more sodium citrate is added in proportion. The citrated blood is then strained through gauze and poured into the infusion apparatus for intravenous injection by the gravity method (see p. 96).

Exsanguination-Transfusion. By exsanguination-transfusion, a very recent therapeutic measure, is meant the simultaneous removal of toxic blood from the patient and its replacement by fresh blood from a healthy donor. It would be expected *a priori* that, in toxemic states, the mechanical dilution of the circulating toxins and the increment of fresh immune bodies and complement would prove of distinct value. Reference has already been made to Robertson's report of two cases of severe carbon monoxide poisoning, in which good results were obtained by simultaneously removing and transfusing one liter of blood (see p. 56).

Recently Robertson[10] has reported results from exsanguination-transfusion in a series of 160 cases of various toxemias of children which would indicate that this procedure had a decided effect in lowering the mortality. The conditions in which Robertson performed this form of therapeutics were (1) the toxemia of severe burns, (2) erysipelas neonatorum, (3) acute intestinal intoxication, (4) resorcin poisoning, (5) malignant scarlet fever and (6) septicemia. The most favorable results were obtained in cases of severe superficial burns and of erysipelas of the newborn, in which conditions the mortality was just about cut in half.

Technic. The amount of blood to be transfused is roughly

estimated on the basis of 35 c.c. per pound of body weight. The quantity of blood thus obtained is about equal to the total amount in the patient's circulation. The blood is obtained from the donor in the manner described for the citrate method of blood transfusion (see p. 96). Robertson, however, recommends that the blood from the donor be received into 100 c.c. glass syringes, each of which contains 10 c.c. of freshly prepared 3.5 per cent sodium citrate solution. Each syringe, when filled, is inverted several times so as to insure proper mixing, and its contents are then emptied into a basin. In the interval, this blood is kept at a temperature of approximately 100° F. by means of a water bath.

Attention is next turned to the recipient. A suitable vein is selected for the transfusion, usually the median basilic; the vein is then exposed and the needle inserted and tied in place. Saline solution is slowly introduced in order to avoid coagulation. The exsanguination needle is then inserted. In very young infants, Robertson recommends puncture of the superior longitudinal sinus (see p. 123 for method), using a guarded needle with a short bevel.

When the anterior fontanelle is closed, the femoral vein is utilized as follows: The saphenous vein is exposed and picked up just before it perforates the cribriform fascia. A large cannula with a short bevel is then inserted into the saphenous vein and pushed along its course until it enters the femoral vein. By this means, it is possible to rapidly remove a large quantity of blood without danger to the circulation of the limb, such as would follow if the femoral vein itself were opened and tied. After its bevel has entered the femoral vein, the needle is tied in the saphenous vein.

The superficial veins of children are not so satisfactory

for producing exsanguination as the superior longitudinal sinus or the femoral vein, as they cannot be relied upon to give a rapid and continuous flow of blood.

The exsanguination of the patient is begun before the transfusion. The amount of blood thus withdrawn depends on the clinical condition of the patient. In small children it is usually from 60 c.c. to 160 c.c. As soon as the pulse shows any sign of weakening, the transfusion is begun. If it should appear that the preliminary withdrawal has gone too close to the margin of safety, 5 to 10 drops of 1:1000 adrenalin solution should be administered by thrusting a hypodermic needle through the rubber tubing connecting the transfusion syringe with the needle in the vein. One of the 100 c.c. glass syringes, filled with citrated blood from the donor, is connected with the transfusion cannula and the infusion is commenced. The exsanguination and the transfusion are carried on *pari passu* until all of the available blood for the transfusion has been used up. As a rule, it is wise to introduce about 100 to 150 c.c. more blood than is removed. If there should be cyanosis or other signs of a failing circulation prior to the exsanguination-transfusion, however, it is a better plan to remove a little more blood than is injected.

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